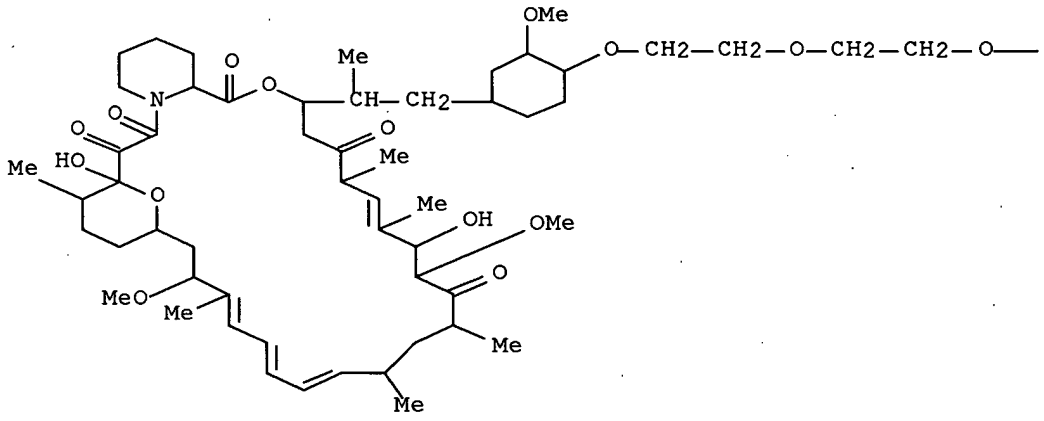
L6 ANSWER 1 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:570556 CAPLUS Full-text
TI Coating comprising poly(butylene terephthalate-co-ethylene glycol) for implantable medical devices
IN Hossainy, Syed F. A.; Tang, Yiwen; Tung, Andrew C.; Pacetti, Stephen D.
PA USA
SO U.S. Pat. Appl. Publ., 8 pp., Division of U.S. Ser. No. 375,620.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005143808	A1	20050630	US 2005-67375	20050225
PRAI US 2003-375620	A3	20030226		

AB An implantable medical device, such as a stent, is disclosed having a coating. The coating includes a poly(butylene terephthalate-co-ethylene glycol) polymer. The coating can also include a drug.
IT **855652-10-7**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coating comprising poly(butylene terephthalate-co-ethylene glycol) for implantable medical devices)
RN 855652-10-7 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

PAGE 1-A



PAGE 1-B

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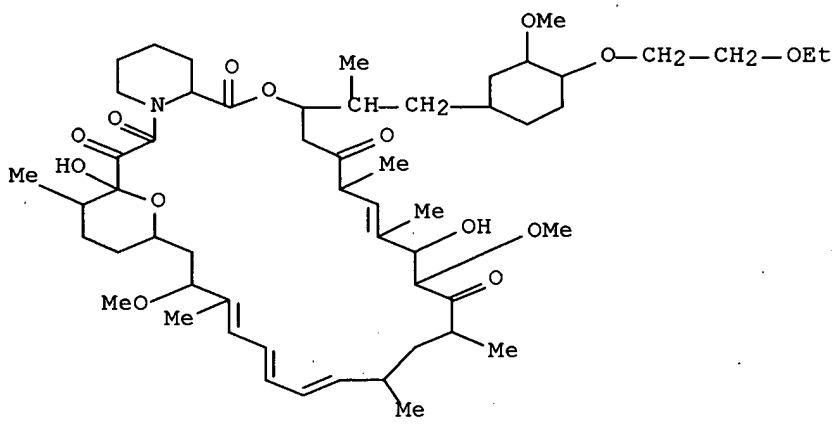
App's

L6 ANSWER 2 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:527394 CAPLUS Full-text
DN 143:48150
TI Compositions containing 42-O-alkoxyalkyl rapamycin derivatives
IN Betts, Ronald E.; Savage, Douglas R.; Shulze, John E.
PA Sun Biomedical, Ltd., USA
SO U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U.S. Ser. No. 706,055.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

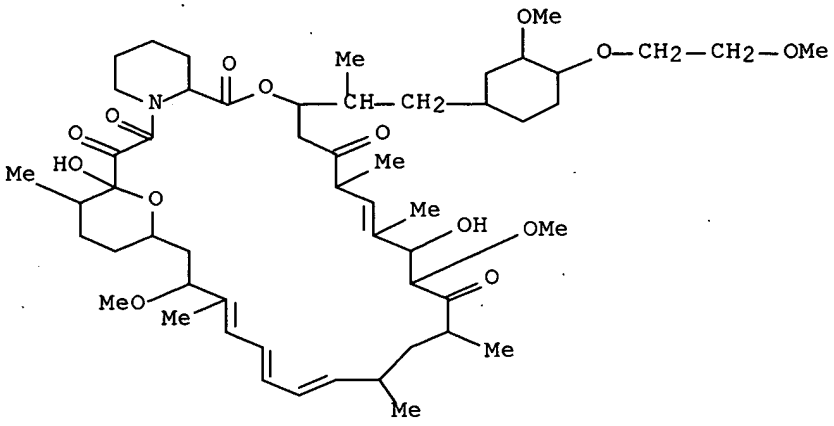
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005131008	A1	20050616	US 2004-987771	20041112
	US 2005101624	A1	20050512	US 2003-706055	20031112
PRAI	US 2003-706055	A2	20031112		

AB 42-O-alkoxyalkyl derivs. of rapamycin having biol. activity are described. Compns. and delivery devices comprising the 42-O-alkoxyalkyl rapamycin derivs. are also disclosed. Thus, 42-O-(2-ethoxyethyl)rapamycin was prepared starting from rapamycin and 2-ethoxyethanol triflate and added to a polylactide solution This was then dispensed on a stent and evaporation of the solvent gave a uniform coating of the polymer-containing drug on the stent.

IT **851536-75-9P**, Biolimus A9
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(compns. comprising alkoxyalkyl rapamycin derivs.)
RN 851536-75-9 CAPLUS
CN Rapamycin, 42-O-(2-ethoxyethyl)- (9CI) (CA INDEX NAME)



IT **169288-19-1P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(compns. comprising alkoxyalkyl rapamycin derivs.)
RN 169288-19-1 CAPLUS
CN Rapamycin, 42-O-(2-methoxyethyl)- (9CI) (CA INDEX NAME)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L6 ANSWER 3 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:493568 CAPLUS Full-text
DN 143:48169
TI Implantable sensors and pumps and anti-scarring agents
IN Hunter, William L.; Gravett, David M.; Toleikis, Philip M.; Maiti, Arpita
PA Angiotech International A.-G., Switz.
SO PCT Int. Appl., 1619 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 12

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005051871	A2	20050609	WO 2004-US39387	20041122
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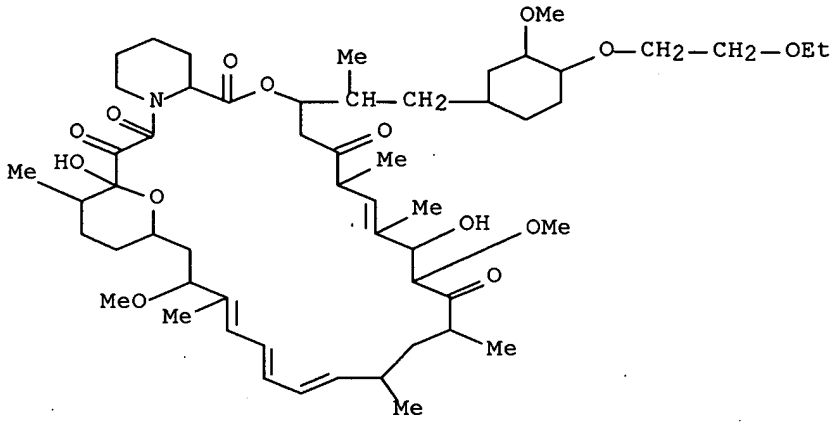
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2005148512	A1	20050707	US 2004-986230	20041110
	US 2005149158	A1	20050707	US 2004-409	20041129
	US 2005142163	A1	20050630	US 2004-1422	20041201
	US 2005143817	A1	20050630	US 2004-6899	20041207
	US 2005147562	A1	20050707	US 2004-6886	20041207
	US 2005147599	A1	20050707	US 2004-6889	20041207
	US 2005147643	A1	20050707	US 2004-6893	20041207
	US 2005154374	A1	20050714	US 2004-6882	20041207
	US 2005152946	A1	20050714	US 2004-6894	20041207
PRAI	US 2003-523908P	P	20031120		
	US 2003-524023P	P	20031120		
	US 2003-525226P	P	20031124		
	US 2003-526541P	P	20031203		
	US 2004-578471P	P	20040609		
	US 2004-586861P	P	20040709		
	US 2004-986230	A	20041110		
	US 2004-986231	A	20041110		
	US 2003-518785P	P	20031110		
	US 2004-996352	A1	20041122		

AB Pumps and sensors for contact with tissue are used in combination with an anti-scarring agent (e.g., a cell cycle inhibitor) in order to inhibit scarring that may otherwise occur when the pumps and sensors are implanted within an animal are disclosed. Thus, a drug-coated device was coated with a heparin coating and dipped into a solution of heparin-benzalkonium chloride complex in isopropanol. The device was removed from the solution and air-dried.

IT **851536-75-9**, Biolimus A9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Biolimus A9; implantable sensors and pumps and anti-scarring agents)
RN 851536-75-9 CAPLUS
CN Rapamycin, 42-O-(2-ethoxyethyl)- (9CI) (CA INDEX NAME)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L6 ANSWER 4 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:493532 CAPLUS Full-text
DN 143:32339
TI Polymer compositions comprising a antifibrotic or an antiinfective agent
IN Hunter, William L.; Gravett, David M.; Toleikis, Philip M.; Maiti, Arpita; Liggins, Richard T.; Takacs-Cox, Aniko; Avelar, Rui; Loss, Troy A. E.
PA Angiotech International A.-G., Switz.
SO PCT Int. Appl., 1945 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 12

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005051452	A2	20050609	WO 2004-US39389	20041122
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	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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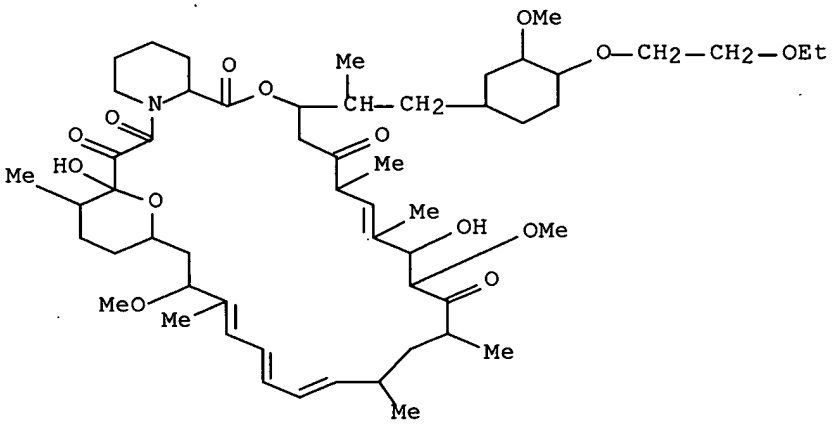
	US 2005142163	A1	20050630	US 2004-1422	20041201
	US 2005143817	A1	20050630	US 2004-6899	20041207
	US 2005147562	A1	20050707	US 2004-6886	20041207
	US 2005147599	A1	20050707	US 2004-6889	20041207
	US 2005147643	A1	20050707	US 2004-6893	20041207
	US 2005154374	A1	20050714	US 2004-6882	20041207
	US 2005152946	A1	20050714	US 2004-6894	20041207
PRAI	US 2003-523908P	P	20031120		
	US 2003-525226P	P	20031124		
	US 2003-526541P	P	20031203		
	US 2004-566569P	P	20040428		
	US 2004-586861P	P	20040709		
	US 2004-611077P	P	20040917		
	US 2004-986231	A	20041110		
	US 2003-518785P	P	20031110		
	US 2003-524023P	P	20031120		
	US 2004-578471P	P	20040609		
	US 2004-986230	A1	20041110		
	US 2004-996352	A1	20041122		

AB Polymer compns. comprise a therapeutic agents such as antifibrotic or an antiinfective agent. Microspheres of mycophenolic acid-PVA were prepared and the average particle size distribution was determined
IT **851536-75-9**, Biolimus A9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymer compns. comprising antifibrotic or antiinfective agent)
RN 851536-75-9 CAPLUS
CN Rapamycin, 42-O-(2-ethoxyethyl)- (9CI) (CA INDEX NAME)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L6 ANSWER 5 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:493530 CAPLUS Full-text
DN 143:32415
TI Soft tissue implants and anti-scarring agents
IN Hunter, William L.; Gravett, David M.; Toleikis, Philip M.; Maiti, Arpita
PA Angiotech International A.-G., Switz.
SO PCT Int. Appl., 2592 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 12

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005051444	A2	20050609	WO 2004-US39465	20041122
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	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2005148512	A1	20050707	US 2004-986230	20041110
	US 2005149158	A1	20050707	US 2004-409	20041129
	US 2005142163	A1	20050630	US 2004-1422	20041201
	US 2005143817	A1	20050630	US 2004-6899	20041207
	US 2005147562	A1	20050707	US 2004-6886	20041207
	US 2005147599	A1	20050707	US 2004-6889	20041207
	US 2005147643	A1	20050707	US 2004-6893	20041207
	US 2005154374	A1	20050714	US 2004-6882	20041207
	US 2005152946	A1	20050714	US 2004-6894	20041207
PRAI	US 2003-523908P	P	20031120		
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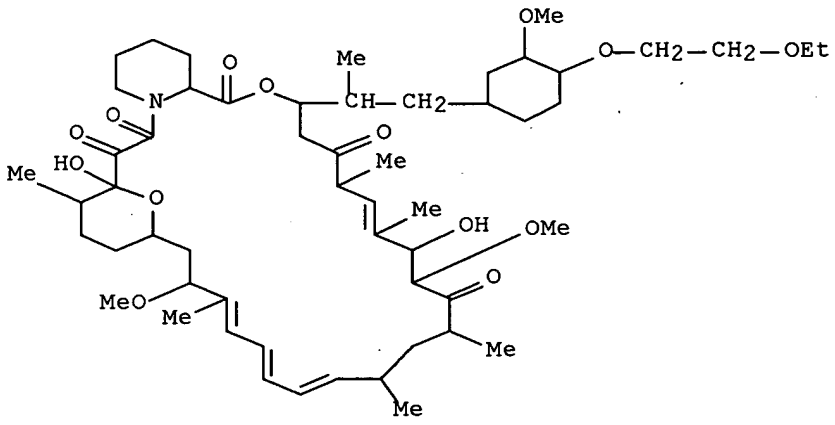
	US 2003-525226P	P	20031124		
	US 2003-526541P	P	20031203		
	US 2004-578471P	P	20040609		
	US 2004-586861P	P	20040709		
	US 2004-986230	A	20041110		
	US 2004-986231	A	20041110		
	US 2003-518785P	P	20031110		
	US 2004-996352	A1	20041122		

AB The invention relates to soft tissue implants for use in cosmetic or reconstructive surgery and to compns. to make the implants resistant to growth by inflammatory scar tissue. Thus, a silicone gel containing paclitaxel was used as a filling in breast implant.

IT **851536-75-9**, Biolimus A9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(soft tissue implants and anti-scarring agents)

RN 851536-75-9 CAPLUS
CN Rapamycin, 42-O-(2-ethoxyethyl)- (9CI) (CA INDEX NAME)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L6 ANSWER 6 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:445853 CAPLUS Full-text
DN 142:469406
TI Rate limiting barriers for implantable devices
IN Hossainy, Syed F. A.
PA Advanced Cardiovascular Systems, Inc., USA
SO U.S., 9 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6896965	B1	20050524	US 2002-293064	20021112
PRAI	US 2002-293064		20021112		

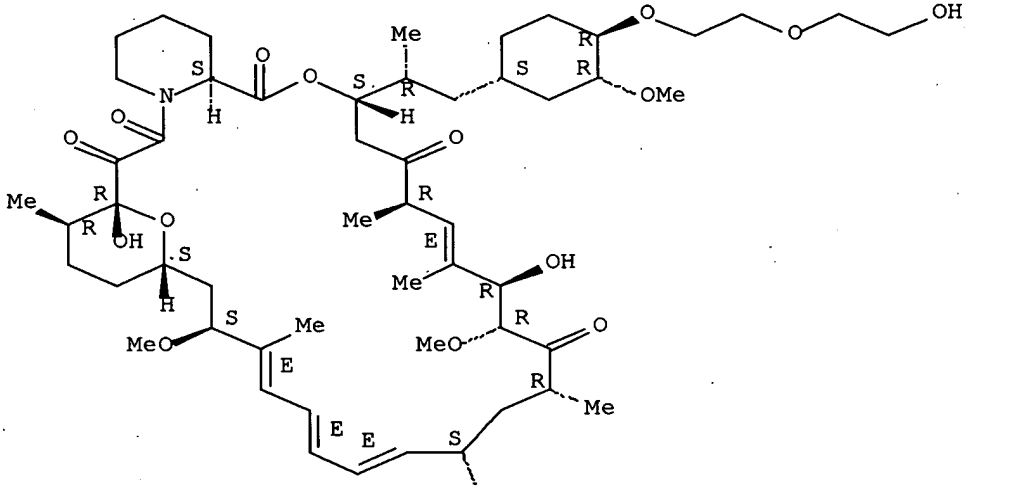
AB A coating for implantable medical devices including an interpenetrating polymer network serving as a rate limiting barrier.

IT **159351-77-6,** 40-O-[2-(2-Hydroxy)ethoxy]ethyl-rapamycin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rate limiting barriers for implantable devices)

RN 159351-77-6 CAPLUS
CN Rapamycin, 42-O-[2-(2-hydroxyethoxy)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 2-A

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:431436 CAPLUS Full-text
DN 142:482787
TI Block copolymers containing fluorinated blocks for use in coating compositions for drug-eluting stents
IN Claude, Charles D.
PA USA
SO U.S. Pat. Appl. Publ., 10 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005107531	A1	20050519	US 2003-714111	20031114
WO 2005049678	A2	20050602	WO 2004-US37474	20041110

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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

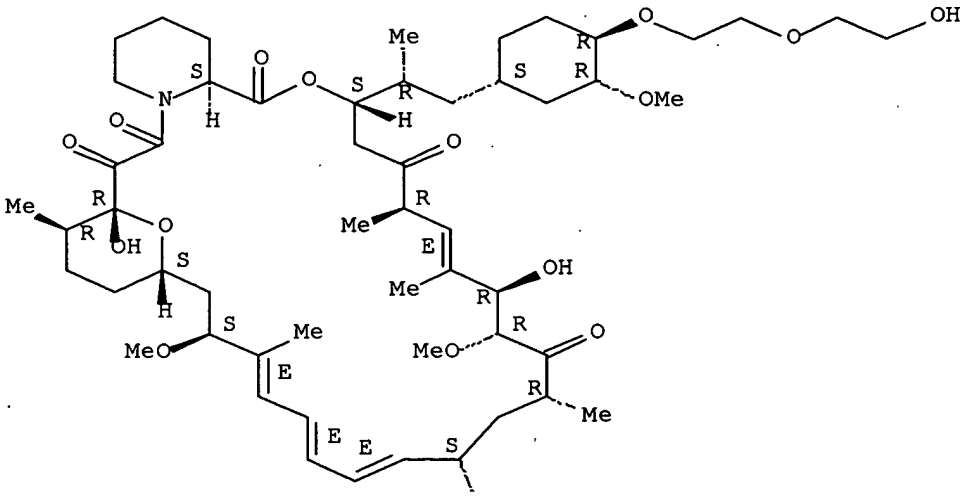
PRAI US 2003-714111 A 20031114

AB A block copolymer comprises a fluorinated block and at least one nonfluorinated block, the fluorinated block having the general structure -[CF2-CH2-CF2-CF(CF3)]n-, and the nonfluorinated block having the general structure -[CH2-C(R1)(R2)]m-, R1 being selected from -CH3, -CF3, -CH2CH3, -CH2CH2CH3, -CH2CH2CH2CH3, Ph, naphthyl, -COOR3, and -CONR3R4; R2 being selected from -H, -CH3, -CF3, -CH2CH3, -CH2CH2CH3, -CH2CH2CH2CH3, Ph, and naphthalenyl; and R3 and R4 being selected from -CH3, -CH2CH3, -CH2CH2CH3, -CH2CH2CH2CH3, -CH2CH2OH, and -PEG. In another embodiment, a block copolymer comprises a fluorinated block and at least one nonfluorinated block, the fluorinated block having the general structure -[CF2-CH2-CF2-CF(CF3)]n-, and the nonfluorinated block being a polymer selected from polyesters, polyethers, polyanhydrides, polyglycols, polyoxyalkylenes, polyhydroxyalkanoates, polyphosphazenes, and polyurethanes. The block copolymers are useful as biocompatible coatings for implantable devices, such as drug-eluting stents, to effect a controlled delivery of an active agent in stent medication.

IT **159351-77-6**, 40-O-[2-(2-Hydroxy)ethoxy]ethyl-rapamycin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(implants for delivery of; block copolymers containing fluorinated blocks for use in coating compns. for drug-eluting stents)

RN 159351-77-6 CAPLUS
CN Rapamycin, 42-O-[2-(2-hydroxyethoxy)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L6 ANSWER 8 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:409234 CAPLUS Full-text
DN 142:463507
TI Preparation of 42-O-alkoxyalkyl rapamycin derivatives and polymer compositions comprising same
IN Betts, Ronald E.; Savage, Douglas R.; Shulze, John E.
PA USA
SO U.S. Pat. Appl. Publ., 26 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005101624	A1	20050512	US 2003-706055	20031112
	WO 2005047295	A1	20050526	WO 2004-US37701	20041112
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	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2005131008	A1	20050616	US 2004-987771	20041112
PRAI	US 2003-706055	A2	20031112		
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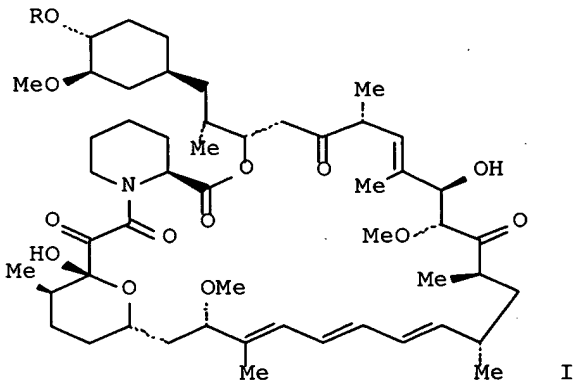


I

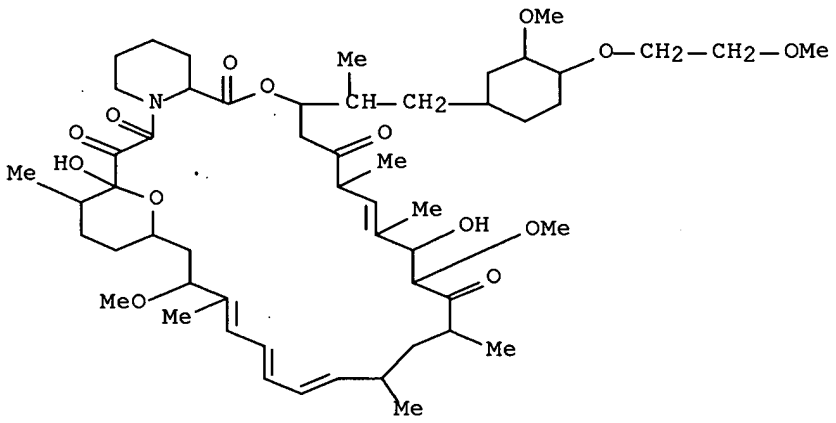
AB 42-O-Alkoxyalkyl derivs. of rapamycin, such as I [R = Ra-O-Rb; Ra = alkylene, alkyl; Rb = alkyl], were prepared for their use in a polymer composition for treating conditions responsive to treatment by rapamycin. Compns. and delivery devices comprising I are also disclosed.

IT **169288-19-1P 851536-75-9P**, Biolimus A9
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 42-O-alkoxyalkyl rapamycin derivs. and polymer compns. containing same)

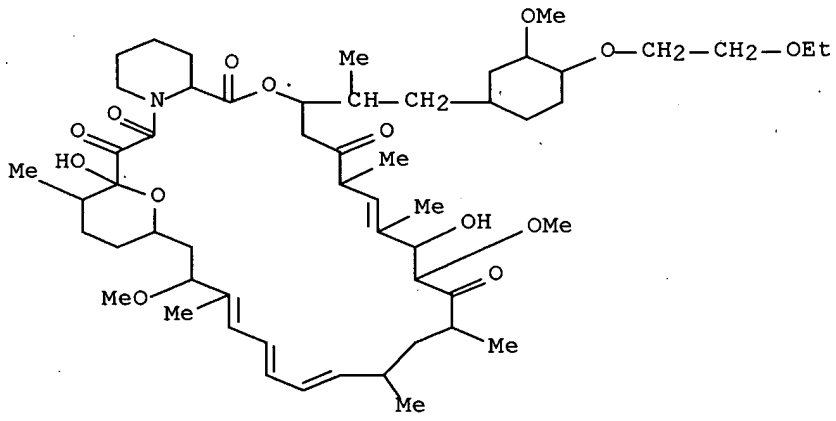
RN 169288-19-1 CAPLUS

CN Rapamycin, 42-O-(2-methoxyethyl)- (9CI) (CA INDEX NAME)



RN 851536-75-9 CAPLUS

CN Rapamycin, 42-O-(2-ethoxyethyl)- (9CI) (CA INDEX NAME)

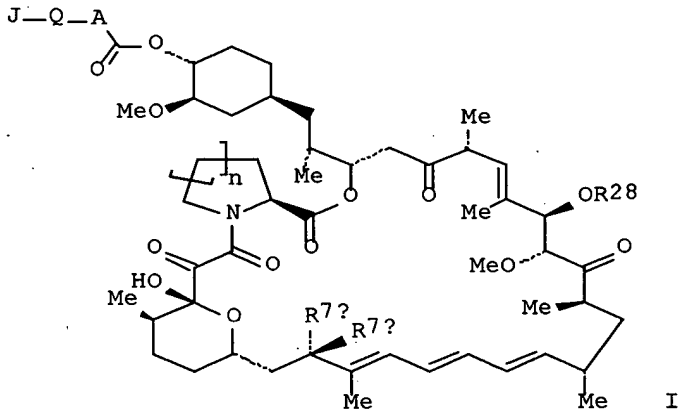


L6 ANSWER 9 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:99140 CAPLUS Full-text
DN 142:176610
TI Preparation of phosphorus-containing rapamycin derivatives for use in pharmaceutical compositions as anticancer and antiresorptive agents
IN Metcalf, Chester A.; Rozamus, Leonard W.; Wang, Yihan
PA USA
SO U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005026868	A1	20050203	US 2004-889163	20040712
WO 2005016252	A2	20050224	WO 2004-US22452	20040712

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-486367P P 20030711
OS MARPAT 142:176610
GI



I

AB Rapamycin derivs. containing a phosphorus moiety, such as I [A = O, S, NR2; Q = bond, aliphatic, heteroaliph., aryl, or heteroaryl moiety; J = C(X){P(O)(OH)2}2, P(O)(OH)CX2P(O)(OH)2; X = H, O-substituted, halo; R2 = H, aliphatic, heteroaliph., heteroaryl; R7a, R7b = H, RA, ORA, SRA, OCORA, OCONRARB, NRARB; RA = R2; RB = OH; R28 = COAQJ; n = 1-2], were prepared for therapeutic use as anticancer and antiresorptive agents. Thus, rapamycin

carbonate I [A-Q-J = OC6H4NO2-4, R7a = OMe, R7b = H, R28 = H, n = 2] prepared by the reaction of rapamycin and 4-nitrophenyl chloroformate, was reacted with alendronic acid to afford rapamycin carbamate derivative I [A-Q-J = NH(CH2)3C(OH){P(O)(OH)2}2, R7a = OMe, R7b = H, R28 = H, n = 2]. Binding affinity of I for human FKBP protein was assayed, dosages for inhibition of osteoclast formation and antiresorptive activity of I in hypercalcemic mice were discussed.

IT **833448-56-9P 833448-58-1P 833448-61-6P**

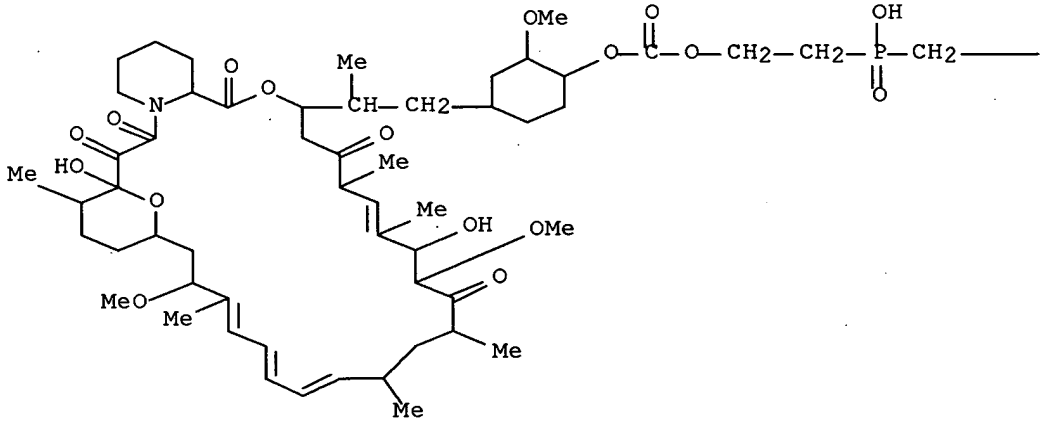
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of phosphorus-containing rapamycin derivs. for use in pharmaceutical compns. for treatment of cancer or disease involving undue bone resorption)

RN 833448-56-9 CAPLUS

CN Rapamycin, 42-[2-[hydroxy(phosphonomethyl)phosphinyl]ethyl carbonate] (9CI) (CA INDEX NAME)

PAGE 1-A



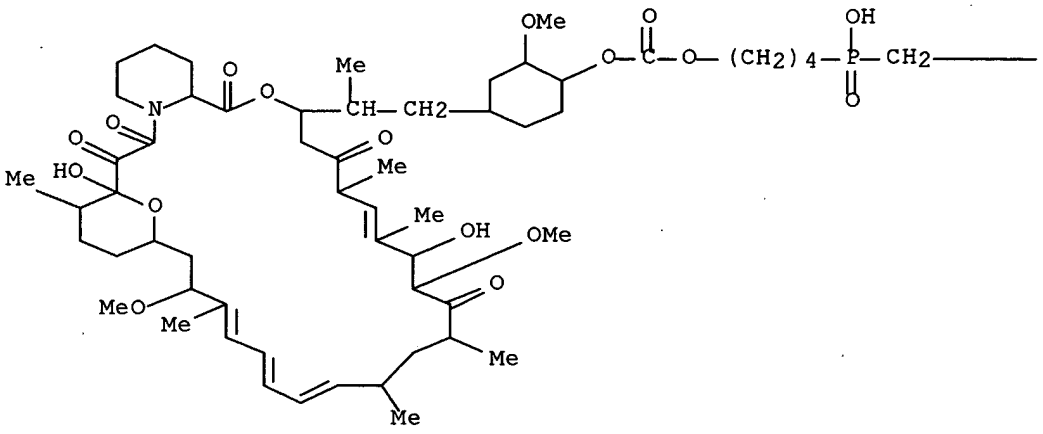
PAGE 1-B

—PO3H2

RN 833448-58-1 CAPLUS

CN Rapamycin, 42-[4-[hydroxy(phosphonomethyl)phosphinyl]butyl carbonate] (9CI) (CA INDEX NAME)

PAGE 1-A

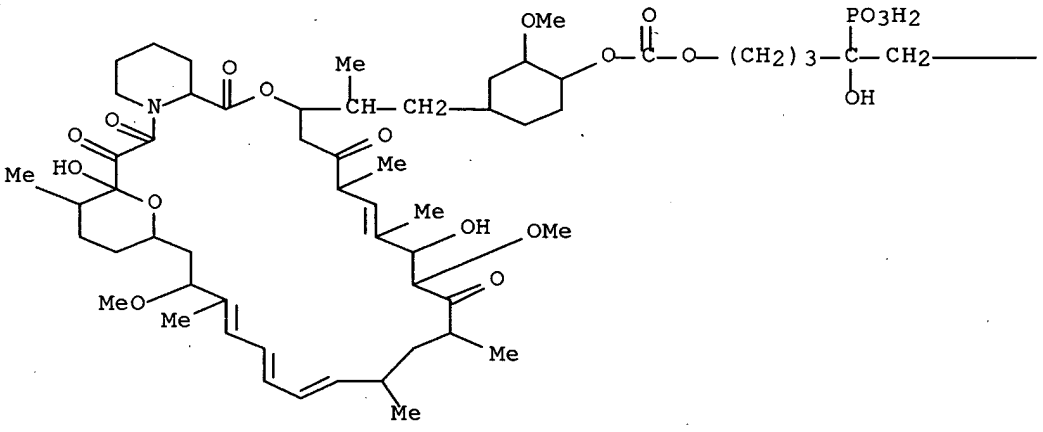


PAGE 1-B

—PO3H2

RN 833448-61-6 CAPLUS
CN Rapamycin, 42-(4-hydroxy-4,5-diphosphonopentyl carbonate) (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

—PO3H2

L6 ANSWER 10 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:964607 CAPLUS Full-text
DN 141:401014
TI Stent coatings comprising hydrophilic additives
IN Pacetti, Stephen D.; Tang, Yiwen
PA USA
SO U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004224001	A1	20041111	US 2003-431711	20030508
	WO 2004101018	A1	20041125	WO 2004-US9011	20040323

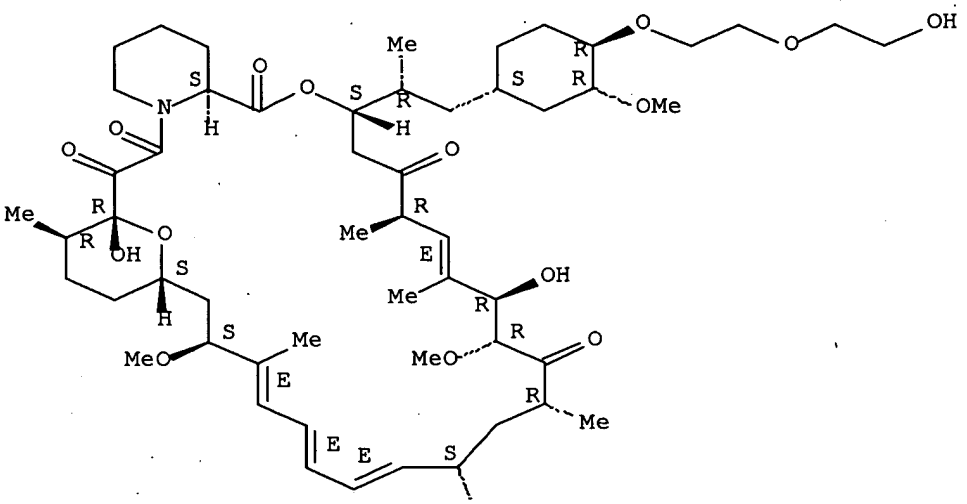
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-431711 A 20030508

AB A coating for implantable medical devices and a method for fabricating thereof are disclosed. The coating includes a mixture of a hydrophobic polymer and a polymeric hydrophilic additive, wherein the hydrophobic polymer and the hydrophilic additive form a phys. entangled or interpenetrating system. For example, a first composition was prepared by mixing 2.0 % of poly(ethylene-co-vinyl alc.) with DMAC solvent balance and applied onto the surface of a bare Vision stent (available from Guidant Corp.) by spraying and dried to form a primer layer. A second composition was prepared by mixing 2.0 % of poly(ethylene-co-vinyl alc.), 1.6 % of Everolimus, and the balance DMAC solvent. The second composition was applied onto the dried primer layer to form a drug-polymer layer. A third composition was prepared by mixing 2 % of poly(Bu methacrylate), 0.1 % of PEG, and a 1:1 by mass mixture of acetone and cyclohexanone and applied onto the dried drug-polymer layer, to form a topcoat layer.

IT **159351-77-6**, 40-O-[2-(2-Hydroxy)ethoxy]ethylrapamycin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coatings for medical implants comprising hydrophobic polymers and hydrophilic additives and drugs)
RN 159351-77-6 CAPLUS
CN Rapamycin, 42-O-[2-(2-hydroxyethoxy)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



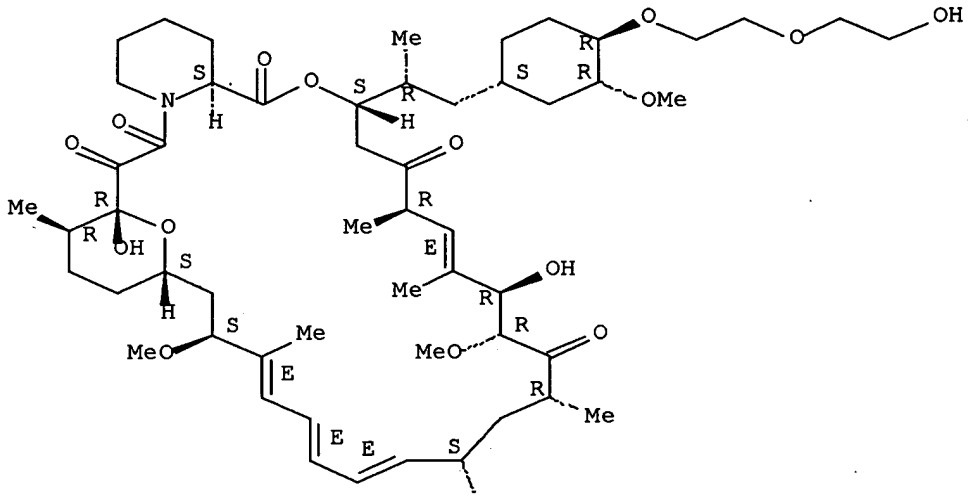
L6 ANSWER 11 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:310844 CAPLUS Full-text
DN 140:327174
TI Rate limiting barriers for implantable medical devices
IN Hossainy, Syed F. A.; Tang, Fuh-Wei; Dehnad, Houdin
PA USA
SO U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004072922	A1	20040415	US 2002-269004	20021009
	WO 2004032804	A1	20040422	WO 2003-US30349	20030924
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1549249	A1	20050706	EP 2003-754901	20030924
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	US 2002-269004	A	20021009		
	WO 2003-US30349	W	20030924		

AB A coating for a medical device, particularly for a drug eluting stent, is described. The coating comprises a polymer having a weight-average mol. weight between about 200,000 and about 250,000 Daltons or a polydispersity index between about 2.6 and about 3.0. Compns. contained, e.g., Eval, Everolimus and dimethylacetamide solvent.

IT **159351-77-6**, 40-O-[2-(2-Hydroxyethoxy)ethyl]rapamycin
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(rate limiting barriers for implantable medical devices)
RN 159351-77-6 CAPLUS
CN Rapamycin, 42-O-[2-(2-hydroxyethoxy)ethyl]- (9CI) (CA INDEX NAME)

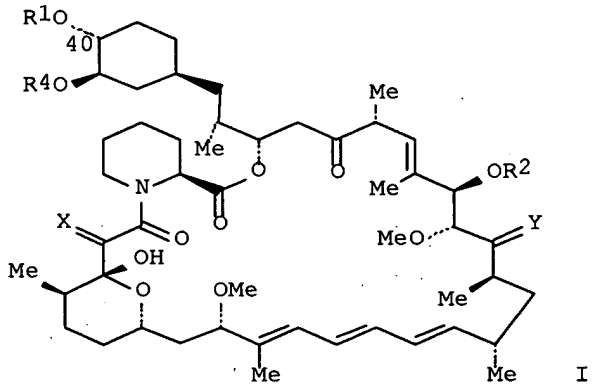
Absolute stereochemistry.
Double bond geometry as shown.



L6 ANSWER 12 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:41124 CAPLUS Full-text
DN 140:93840
TI Rapamycin and O-alkylated rapamycin derivatives for alleviation and inhibition of lymphoproliferative disorders
IN Wasik, Mariusz A.; Shaw, Leslie M.
PA The Trustees of the University of Pennsylvania, USA
SO U.S. Pat. Appl. Publ., 23 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004010002	A1	20040115	US 2002-192193	20020709
PRAI US 2002-192193		20020709		

OS MARPAT 140:93840
GI



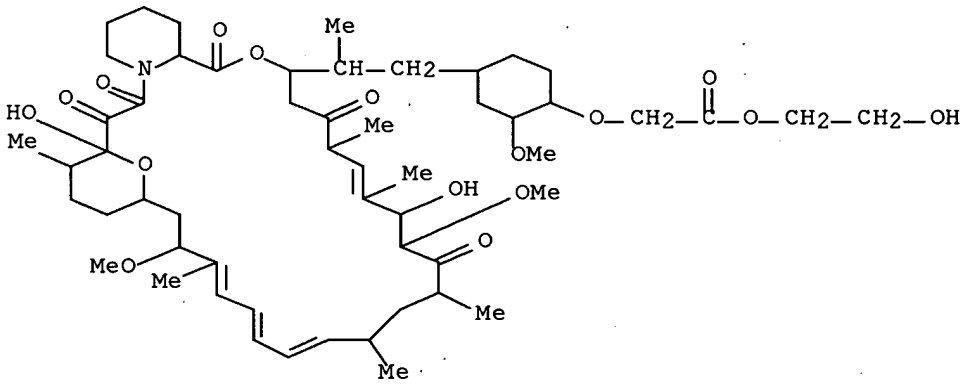
I

AB The present invention relates to methods of alleviating and inhibiting a lymphoproliferative disorder in a mammal, the method comprising administering one or more rapamycin derivs. such as I [X = H2, O; Y = H(OH), O; R1, R2 = H, alkyl, thioalkyl, arylalkyl, hydroxyalkyl, alkoxyalkyl, acyloxyalkyl, aminoalkyl, acylaminoalkyl, arylsulfonamidoalkyl, (R3)3Si; R3= H, Me, Et, iso-Pr, tert-Bu, phenyl; R4 = Me; R1R4 = alkylene], (including rapamycin) to the mammal. Further, the invention provides a method for identifying agents which are useful for alleviating and inhibiting a lymphoproliferative disorders, as well as a method for identifying agents which are capable of inhibiting metastasis of lymphatic tumors in a mammal.

IT **159351-67-4P**, 40-O-(2-Hydroxy)ethoxycarbonylmethylrapamycin
159351-77-6P, 40-O-[2-(2-Hydroxy)ethoxy]ethyl-rapamycin
159351-79-8P, 40-O-(2-Acetoxy)ethylrapamycin **159351-80-1P**
, 40-O-(2-Nicotinoyloxy)ethylrapamycin **159351-82-3P**,
40-O-[2-(N-Morpholino)acetoxy]ethylrapamycin **159351-83-4P**
159351-84-5P, 40-O-[2-(N-Methyl-N'-piperazinyl)acetoxy]ethylrapamy
cin
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(rapamycin and rapamycin derivs. for alleviation and inhibition of lymphoproliferative disorders)

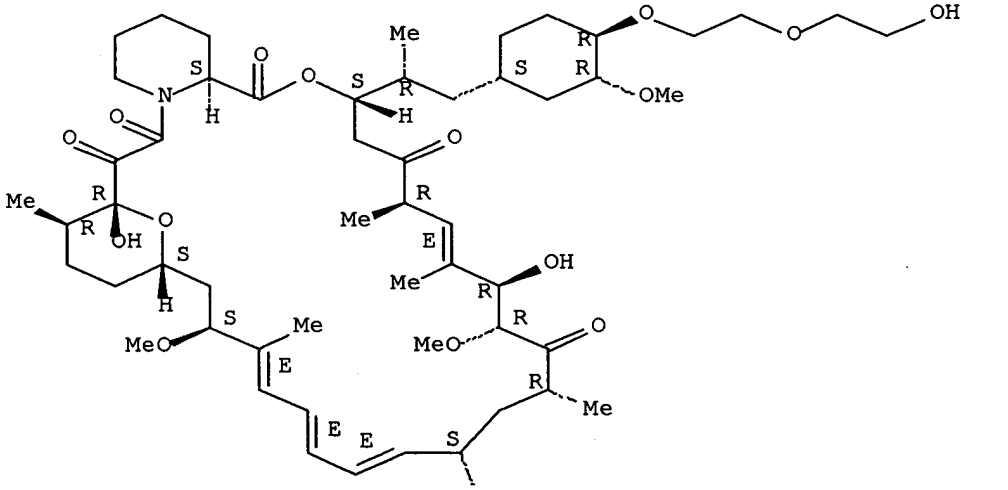
RN 159351-67-4 CAPLUS
CN Rapamycin, 42-O-[2-(2-hydroxyethoxy)-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 159351-77-6 CAPLUS
CN Rapamycin, 42-O-[2-(2-hydroxyethoxy)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

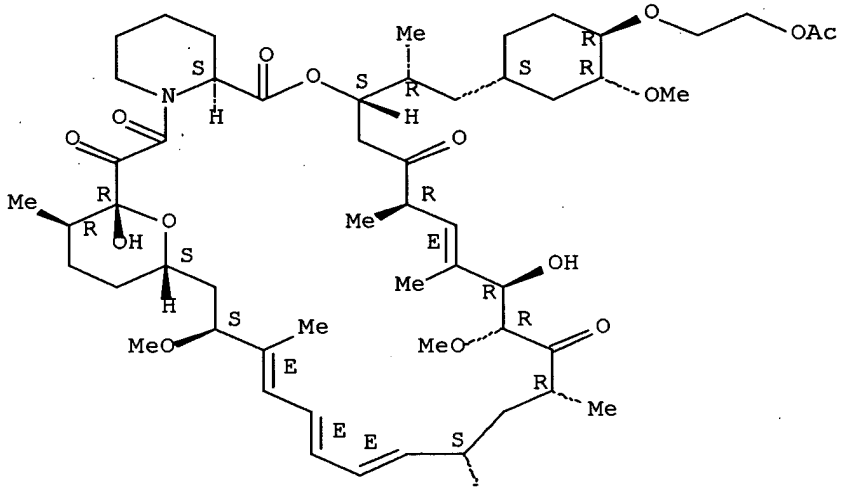


PAGE 2-A

RN 159351-79-8 CAPLUS
CN Rapamycin, 42-O-[2-(acetyloxy)ethyl]- (9CI) (CA INDEX NAME)

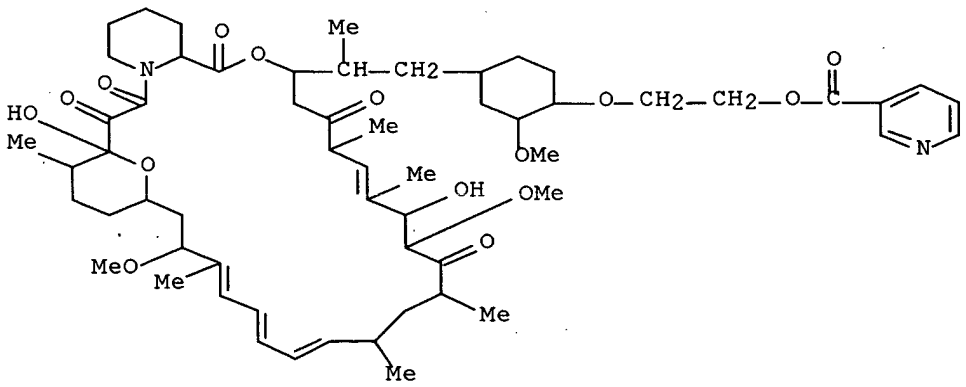
Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



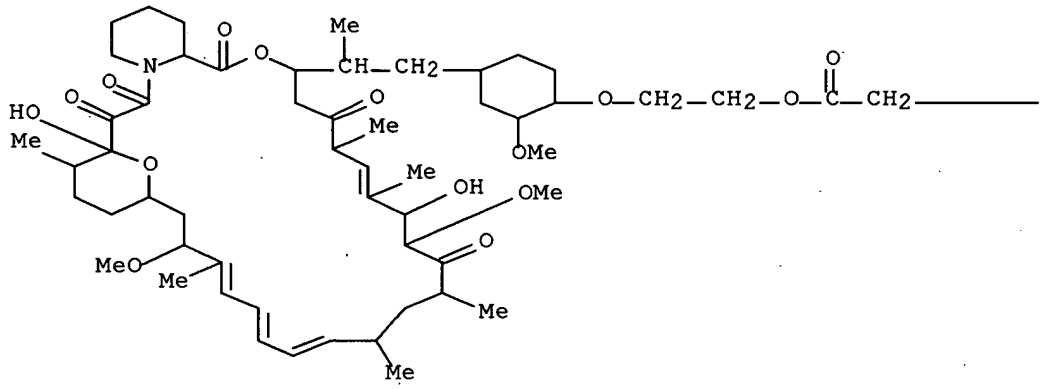
PAGE 2-A

RN 159351-80-1 CAPLUS
CN Rapamycin, 42-O-[2-[(3-pyridinylcarbonyl)oxy]ethyl]- (9CI) (CA INDEX NAME)

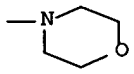


RN 159351-82-3 CAPLUS
CN Rapamycin, 42-O-[2-[(4-morpholinylacetyl)oxy]ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

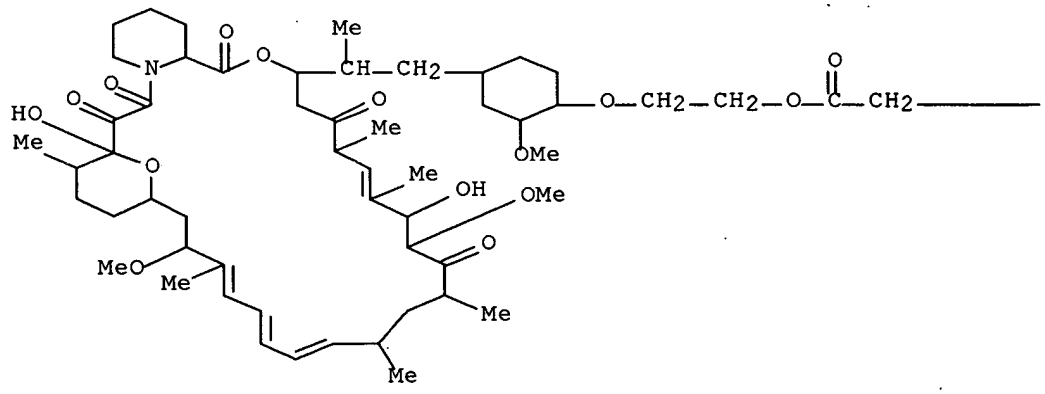


PAGE 1-B

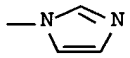


RN 159351-83-4 CAPLUS
CN Rapamycin, 42-O-[2-[(1H-imidazol-1-ylacetyl)oxy]ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

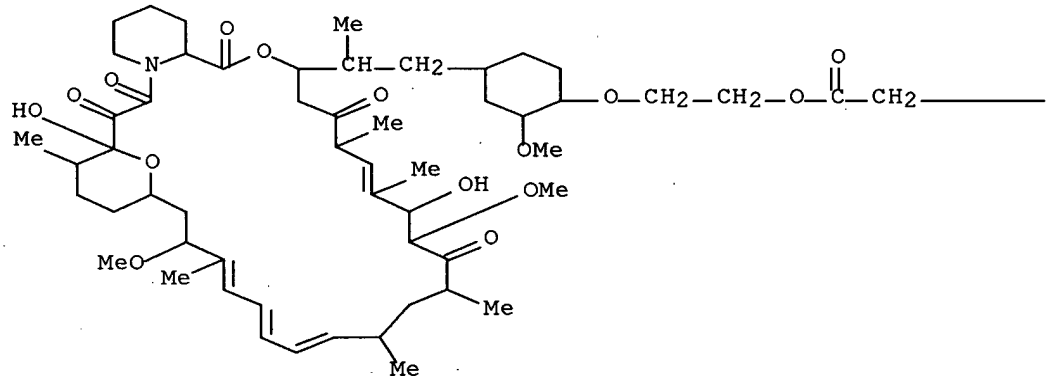


PAGE 1-B

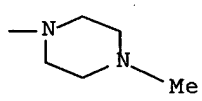


RN 159351-84-5 CAPLUS
CN Rapamycin, 42-O-[2-[[(4-methyl-1-piperazinyl)acetyl]oxy]ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L6 ANSWER 13 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:796548 CAPLUS Full-text
DN 139:312492
TI 40-O-(2-Hydroxy)ethylrapamycin coated stent
IN Hossainy, Syed F. A.; Stewart, Gordon C.; Williams, Mark A.; Royal, Jeff; Consigny, Paul M.; Happ, Dorie M.; Scheinpflug, Kurt; Hu, Ty
PA Advanced Cardiovascular Systems, Inc., USA
SO PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003082368	A1	20031009	WO 2003-US7908	20030313
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1490125	A1	20041229	EP 2003-745538	20030313
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	US 2002-108004	A	20020327		
	WO 2003-US7908	W	20030313		

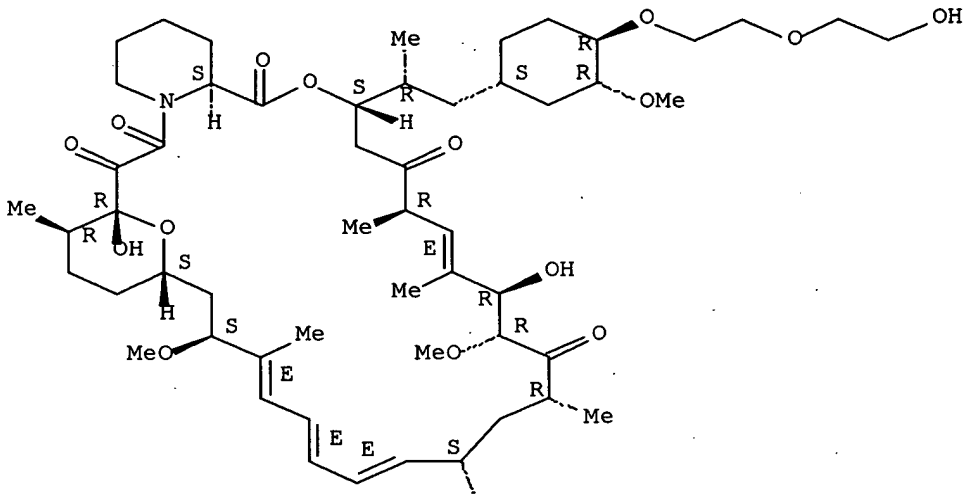
AB A method and coating for reducing the release rate of an active agent from an implantable device, such as a stent, is disclosed. PENTA stents were coated by spraying a 2% solution of poly(ethylene-co-vinyl alc.) (44 mol% ethylene) (EVAL) in 98% dimethylacetamide. The solvent was removed by baking at 140°for 2 h. A solution of 1.9% EVAL and 0.7% 40-O-(2-hydroxy)ethylrapamycin in a mixture of 68.2% dimethylacetamide and 29.2% ethanol was spray coated onto the stents to a thickness with a target of 175 μg 40-O-(2-hydroxy)ethylrapamycin on each stent. A barrier layer was formed by spraying the stents with a 4% solution of EVAL in a mixture of 76% dimethylacetamide and 20% pentane. For the primer layer, there was a target dry weight of 40 μg polymer, and a measured average dry weight of 43μg polymer. For the reservoir layer, the target drug-polymer ratio was 1:2.857, the target dry weight for the entire reservoir coating was 675 μg and the average actual dry weight was 683 μg.

IT **159351-77-6**, 40-O-[2-(2-Hydroxy)ethoxy]ethylrapamycin
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(hydroxyethylrapamycin coated stent)

RN 159351-77-6 CAPLUS
CN Rapamycin, 42-O-[2-(2-hydroxyethoxy)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 2-A

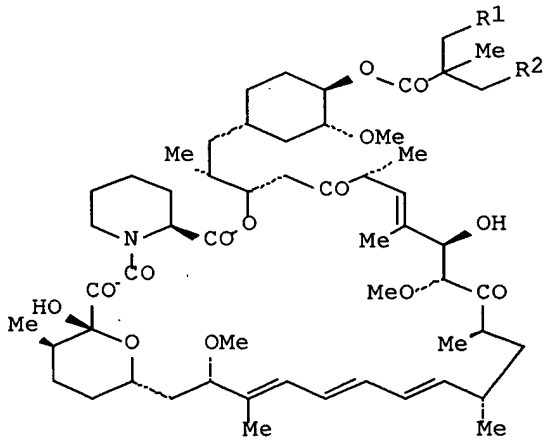
Me

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:240783 CAPLUS Full-text
DN 136:263031
TI Preparation of water soluble rapamycin esters for pharmaceutical use
IN Zhu, Tianmin; Fawzi, Mahdi Bakir
PA American Home Products Corporation, USA
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002024706	A2	20020328	WO 2001-US28575	20010913
	WO 2002024706	A3	20021010		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2421485	AA	20020328	CA 2001-2421485	20010913
	AU 2001090841	A5	20020402	AU 2001-90841	20010913
	EP 1319008	A2	20030618	EP 2001-970890	20010913
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001013975	A	20030729	BR 2001-13975	20010913
	JP 2004509898	T2	20040402	JP 2002-529116	20010913
	US 2002055518	A1	20020509	US 2001-954782	20010918
	US 6432973	B2	20020813		
PRAI	US 2000-233776P	P	20000919		
	WO 2001-US28575	W	20010913		

OS CASREACT 136:263031
GI



I

AB Water soluble sulfur linked rapamycin polyethylene glycol esters, such as I [R1 = OH, R2 = OCOCH2SCH2CH2-(OCH2CH2)n-OMe; R1 = R2 = OCOCH2SCH2CH2-(OCH2CH2)n-OMe], were prepared for use as therapeutic agents for the treatment of diseases, such as transplant rejection, autoimmune diseases, solid tumors, fungal infections, and vascular disease. Thus, rapamycin esters I [R1 = OH, R2 = OCOCH2SCH2CH2-(OCH2CH2)n-OMe; R1 = R2 = OCOCH2SCH2CH2-(OCH2CH2)n-OMe; average n = 180] were prepared via condensation using NaHCO3 in MeCN and H2O of mPEG-SH 5000 with iodoacetate rapamycin derivs. I (R1 = OH, R2 = OCOCH2I; R1 = R2 = OCOCH2I) which had been prepared by esterification of CCI 779 with iodoacetic acid. The rapamycin esters I were tested for inhibition of U87MG human giloblastoma cell growth.

IT **405195-32-6P 405195-33-7P**

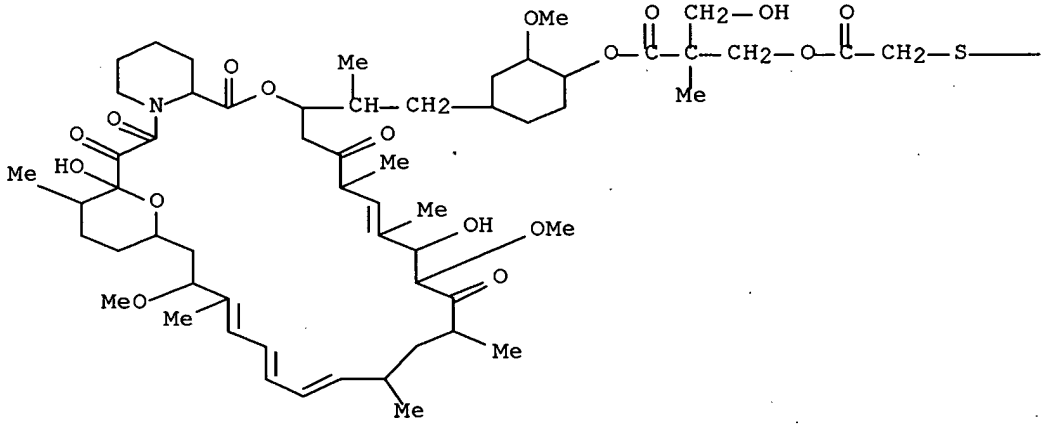
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of water soluble rapamycin esters for pharmaceutical uses, such as antitumor and anti-inflammatory agents)

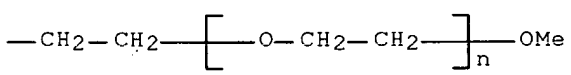
RN 405195-32-6 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-methoxy-, 42-ether with rapamycin 42-[3-hydroxy-2-[[[[(2-hydroxyethyl)thio]acetyl]oxy]methyl]-2-methylpropanoate] (1:1) (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

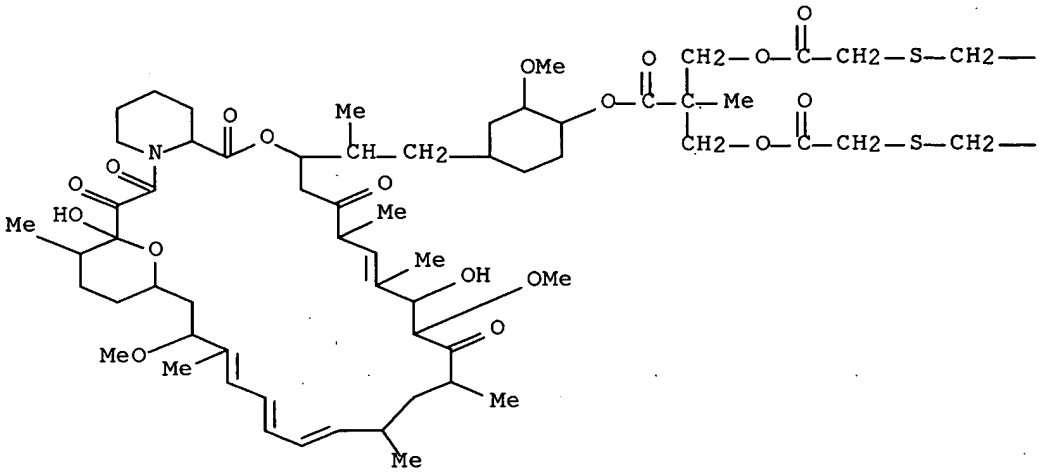


RN 405195-33-7 CAPLUS

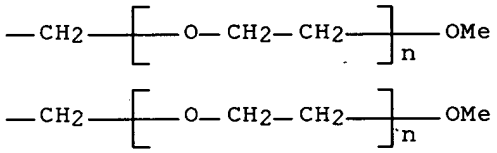
CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-methoxy-, 42-ether with rapamycin 42-[3-[[[(2-hydroxyethyl)thio]acetyl]oxy]-2-[[[[(2-

hydroxyethyl)thio]acetyl]oxy]methyl]-2-methylpropanoate] (2:1) (9CI) (CA INDEX NAME)

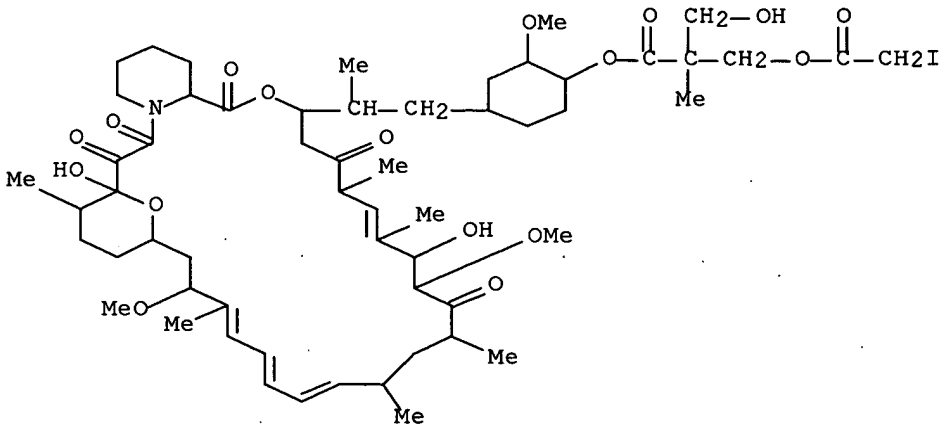
PAGE 1-A



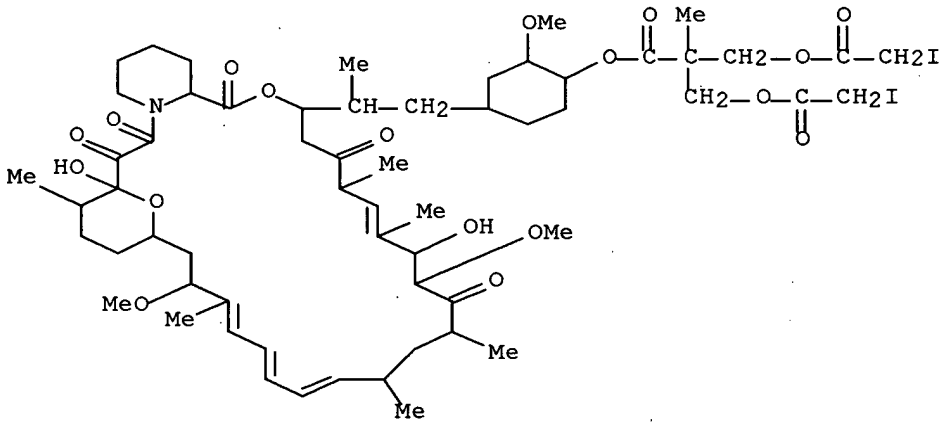
PAGE 1-B



IT **405195-30-4P 405195-31-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of water soluble rapamycin esters for pharmaceutical uses, such as
antitumor and anti-inflammatory agents)
RN 405195-30-4 CAPLUS
CN Rapamycin, 42-[3-hydroxy-2-[[(iodoacetyl)oxy]methyl]-2-methylpropanoate] (9CI) (CA INDEX NAME)



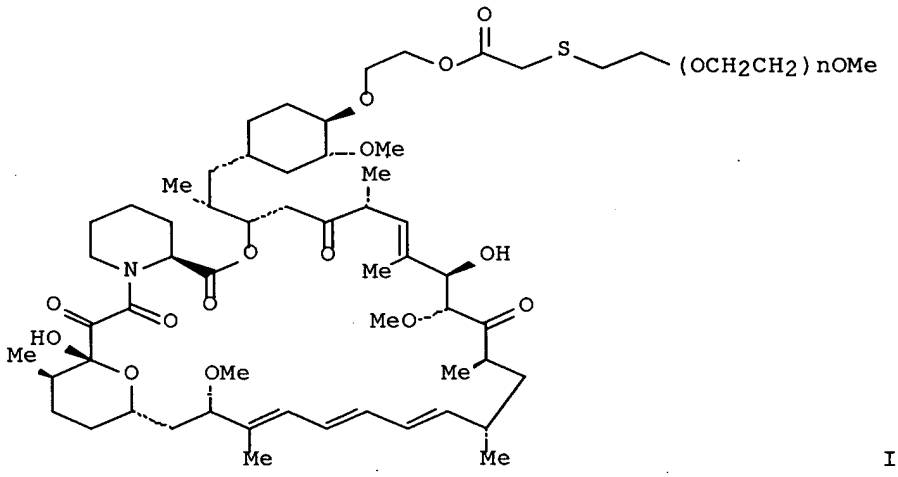
RN 405195-31-5 CAPLUS
CN Rapamycin, 42-[3-[(iodoacetyl)oxy]-2-[[(iodoacetyl)oxy]methyl]-2-methylpropanoate] (9CI) (CA INDEX NAME)



L6 ANSWER 15 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:916408 CAPLUS Full-text
DN 136:37445
TI Synthesis and biological activity of water soluble SDZ-RAD esters
IN Zhu, Tianmin; Shah, Syed M.; Saunders, Richard W.
PA American Home Products Corporation, USA
SO U.S., 8 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6331547	B1	20011218	US 2000-639610	20000816
PRAI US 1999-183035P	P	19990818		

GI



I

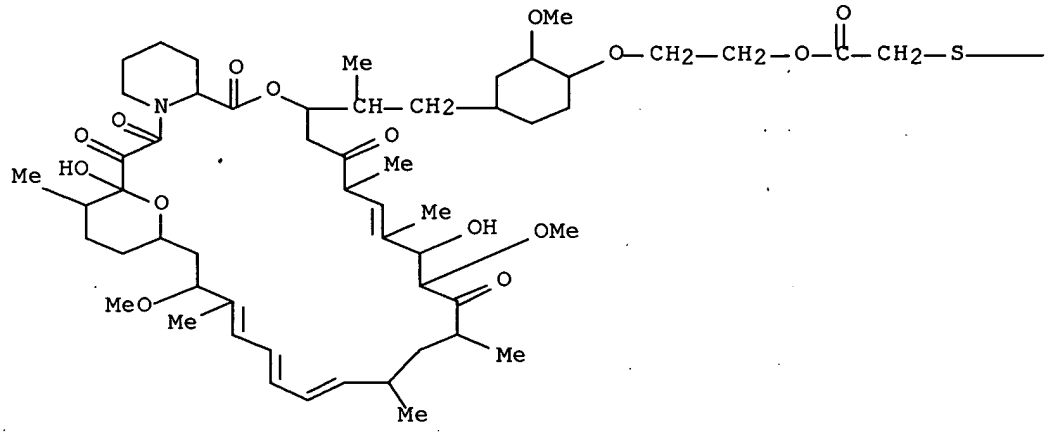
AB This invention provides novel water soluble polyethylene glycol esters of rapamycin [I; n = 5-450] as well as pharmaceutical compns. containing these compds. and methods for their use as immunosuppressive, anti-inflammatory, antifungal, antiproliferative and antitumor agents. Thus, SDZ-RAD was reacted with iodoacetic acid to provide SDZ-RAD-iodoacetic ester which on reaction with mPEG-SH 5000 afforded SDZ-RAD-PEG 5000 conjugate I. I showed IC50 = 0.5ng/mL in U87MG Human Glioblastoma (ATCC HTB-14).

IT **326591-82-6P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antitumor activity of water soluble SDZ-RAD esters)

RN 326591-82-6 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-methyl-ω-hydroxy-, 42-ether with 42-O-[2-[[[(2-hydroxyethyl)thio]acetyl]oxy]ethyl]rapamycin (1:1) (9CI) (CA INDEX NAME)

PAGE 1-A



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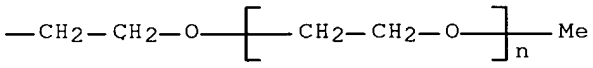
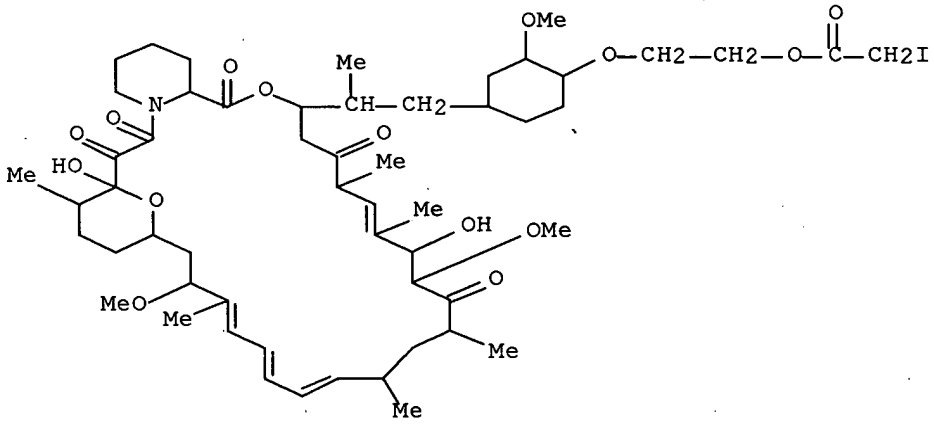


IT **326591-81-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and biol. activity of water soluble SDZ-RAD esters)
RN 326591-81-5 CAPLUS
CN Rapamycin, 42-O-[2-[(iodoacetyl)oxy]ethyl]- (9CI) (CA INDEX NAME)

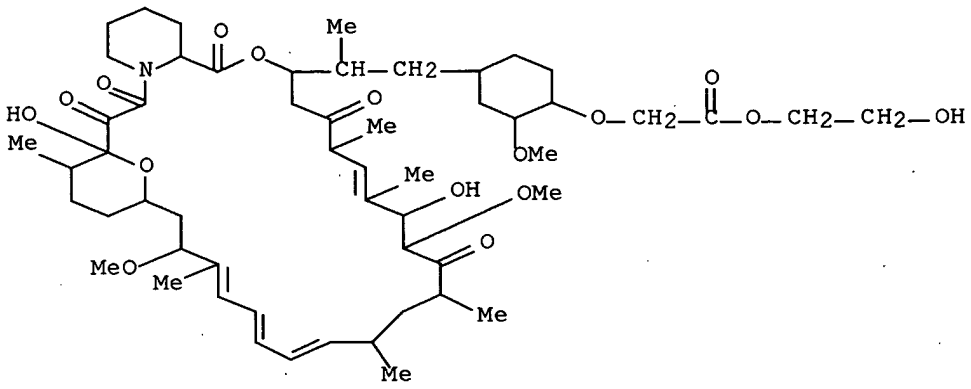


RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:525918 CAPLUS Full-text
DN 135:117214
TI Rapamycin and rapamycin derivatives for alleviation and inhibition of lymphoproliferative disorders
IN Wasik, Mariusz A.; Shaw, Leslie M.
PA The Trustees of the University of Pennsylvania, USA
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001051049	A1	20010719	WO 2001-US1537	20010112
	WO 2001051049	C2	20030116		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2397354	AA	20010719	CA 2001-2397354	20010112
	EP 1250135	A1	20021023	EP 2001-903095	20010112
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003519655	T2	20030624	JP 2001-551473	20010112
PRAI	US 2000-176086P	P	20000114		
	WO 2001-US1537	W	20010112		

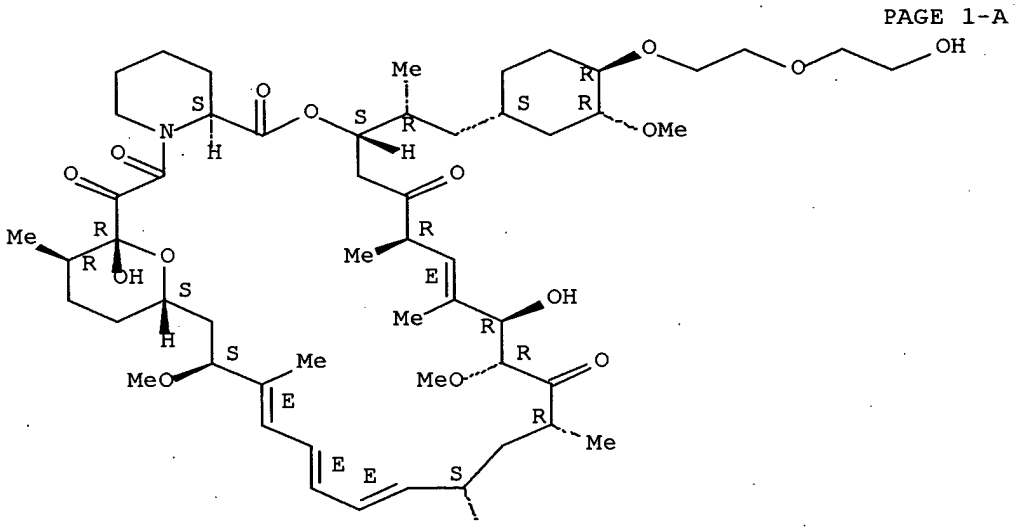
OS MARPAT 135:117214
AB Methods for alleviating and inhibiting a lymphoproliferative disorder in a mammal comprise administering one or more rapamycin derivs. (including rapamycin) to the mammal. The invention also provides a method for identifying agents which are useful for alleviating and inhibiting lymphoproliferative disorders, as well as a method for identifying agents which are capable of inhibiting metastasis of lymphatic tumors in a mammal.
IT **159351-67-4 159351-77-6 159351-79-8**
159351-80-1 159351-82-3 159351-83-4
159351-84-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rapamycin and rapamycin derivs. for treatment of lymphoproliferative disorders)
RN 159351-67-4 CAPLUS
CN Rapamycin, 42-O-[2-(2-hydroxyethoxy)-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 159351-77-6 CAPLUS
CN Rapamycin, 42-O-[2-(2-hydroxyethoxy)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



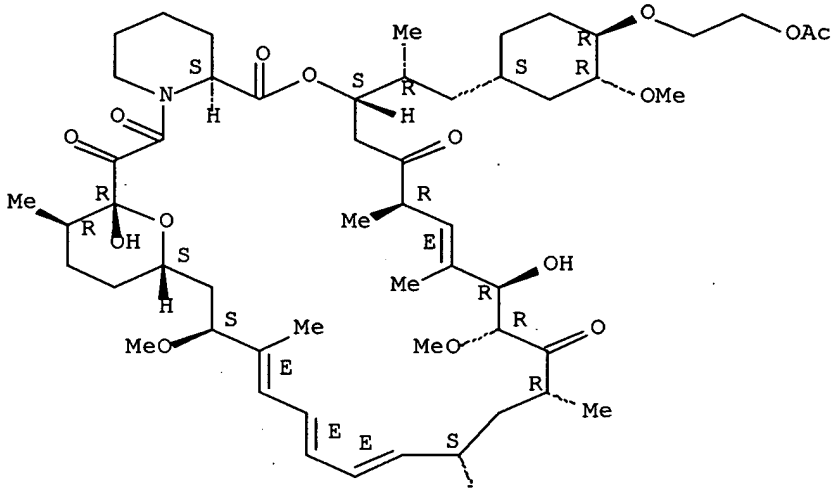
PAGE 2-A

Me

RN 159351-79-8 CAPLUS
CN Rapamycin, 42-O-[2-(acetyloxy)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 2-A

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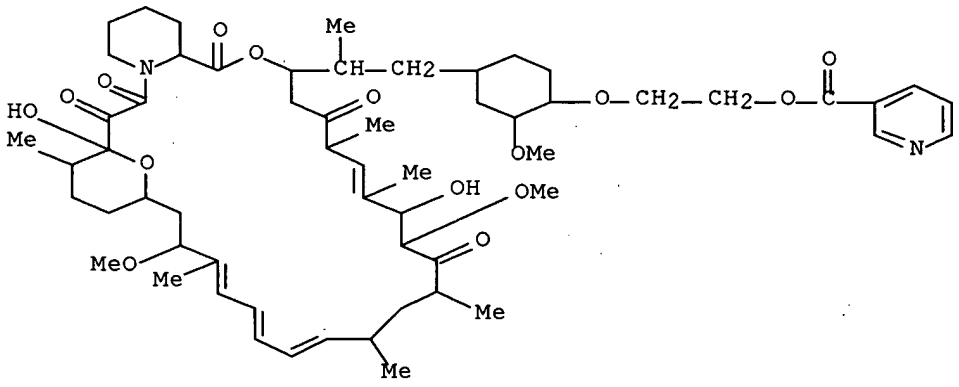
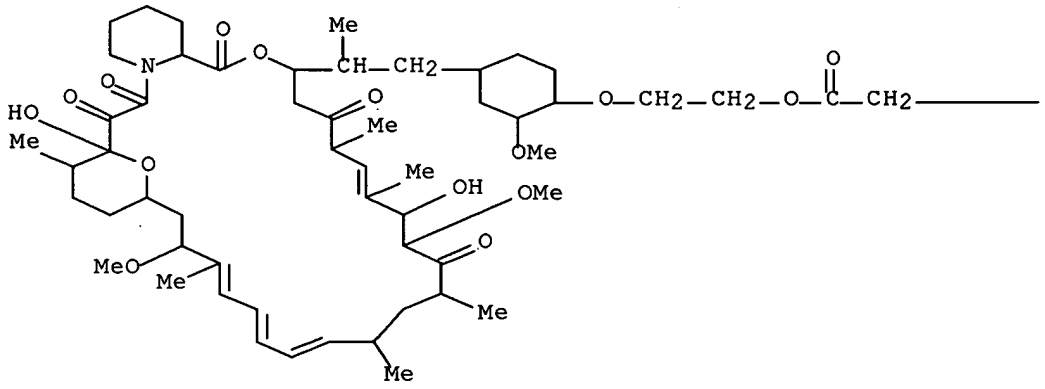
RN 159351-80-1 CAPLUS
CN Rapamycin, 42-O-[2-[(3-pyridinylcarbonyl)oxy]ethyl]- (9CI) (CA INDEX NAME)



RN 159351-82-3 CAPLUS
CN Rapamycin, 42-O-[2-[(4-morpholinylacetyl)oxy]ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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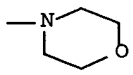
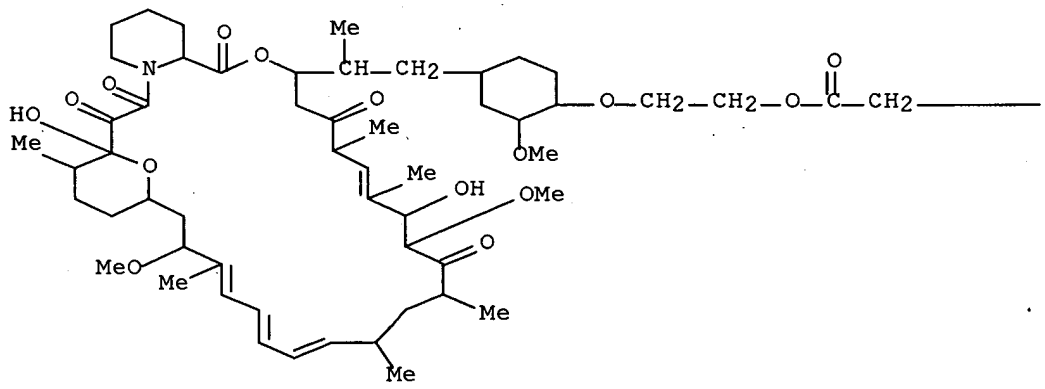
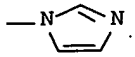


RN 159351-83-4 CAPLUS
CN Rapamycin, 42-O-[2-[(1H-imidazol-1-ylacetyl)oxy]ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

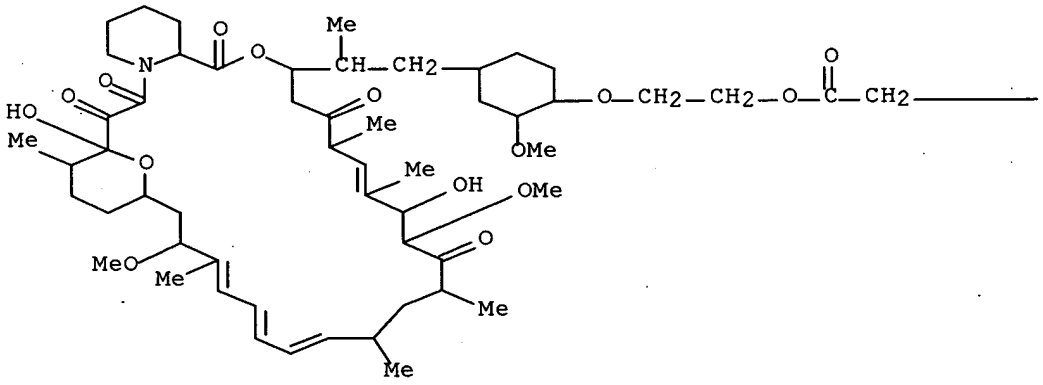


PAGE 1-B



RN 159351-84-5 CAPLUS
CN Rapamycin, 42-O-[2-[[(4-methyl-1-piperazinyl)acetyl]oxy]ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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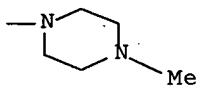
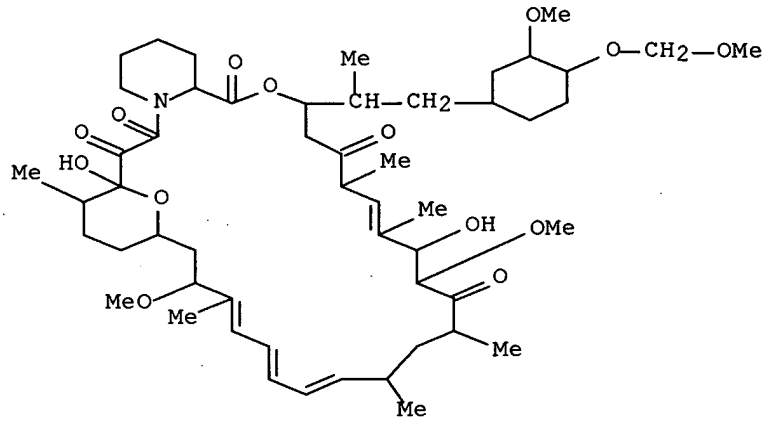


RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:152693 CAPLUS Full-text
DN 134:193290
TI Synthesis and biological activity of 28-epirapalogs with reduced immunosuppressive activity for multimerizing chimeric proteins
IN Yang, Wu; Digits, Cheryl A.; Rozamus, Leonard; Holt, Dennis A.
PA Ariad Gene Therapeutics, Inc., USA
SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001014387	A1	20010301	WO 2000-US23334	20000824
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2383451	AA	20010301	CA 2000-2383451	20000824
	EP 1212331	A1	20020612	EP 2000-959391	20000824
	EP 1212331	B1	20040421		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	AT 264863	E	20040515	AT 2000-959391	20000824
	ES 2219388	T3	20041201	ES 2000-959391	20000824
PRAI	US 1999-150447P	P	19990824		
	WO 2000-US23334	W	20000824		

OS MARPAT 134:193290
AB Methods and materials involving synthesis of 28-epirapamycin analogs are disclosed. Thus, 28-epirapamycin is synthesized via cleavage of rapamycin with titanium tetraisoproxide and retro aldol macrocyclization and analogs are prepared by modification at C7 and C43. These analogs have reduced immunosuppressive activity and comparative data for FKRB binding, activity in cellular transcription assay and activity in mouse splenocyte assay are given.
IT **328059-78-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and biol. activity of 28-epirapalogs with reduced immunosuppressive activity for multimerizing chimeric proteins)
RN 328059-78-5 CAPLUS
CN Rapamycin, 42-O-(methoxymethyl)-, (31S)- (9CI) (CA INDEX NAME)

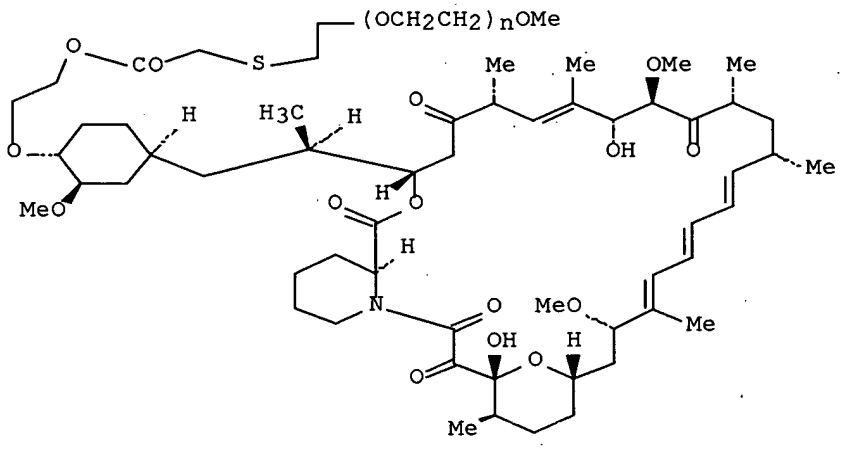


RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:137219 CAPLUS Full-text
DN 134:178401
TI Synthesis and biological activity of water soluble SDZ-RAD esters
IN Zhu, Tianmin; Shah, Syed Muzafar; Saunders, Richard William
PA American Home Products Corporation, USA
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001012633	A1	20010222	WO 2000-US22419	20000816
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2391319	AA	20010222	CA 2000-2391319	20000816
	BR 2000013399	A	20020430	BR 2000-13399	20000816
	EP 1210350	A1	20020605	EP 2000-954091	20000816
	EP 1210350	B1	20040714		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003507382	T2	20030225	JP 2001-517531	20000816
	AT 271052	E	20040715	AT 2000-954091	20000816
	ES 2222222	T3	20050201	ES 2000-954091	20000816
PRAI	US 1999-376685	A	19990818		
	WO 2000-US22419	W	20000816		

GI



I

AB This invention provides novel water soluble polyethylene glycol esters of rapamycin (I) (n = 5-450) as well as pharmaceutical compns. containing these compds. and methods for their use as immunosuppressive, anti-inflammatory, antifungal, antiproliferative and antitumor agents.

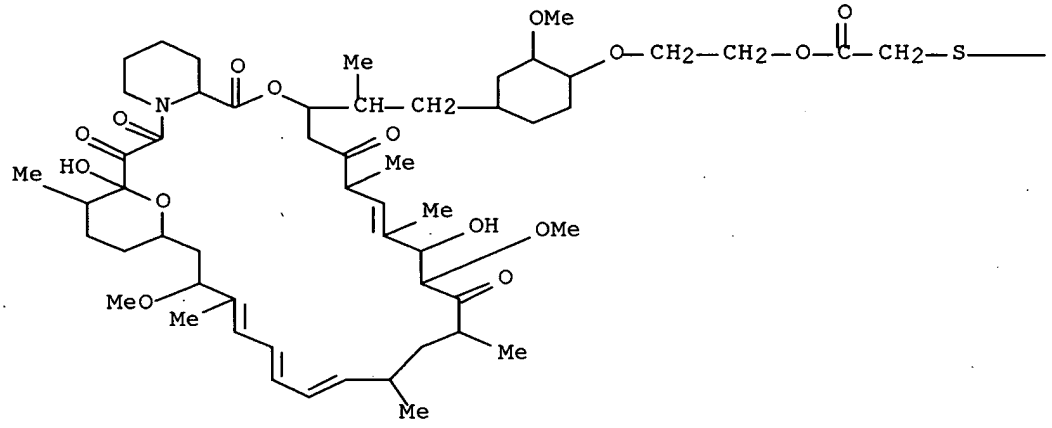
IT **326591-82-6P**

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and biol. activity of water soluble SDZ-RAD esters)

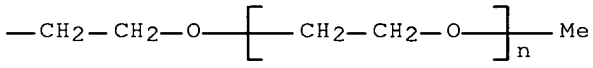
RN 326591-82-6 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-methyl-ω-hydroxy-, 42-ether with 42-O-[2-[[[(2-hydroxyethyl)thio]acetyl]oxy]ethyl]rapamycin (1:1) (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

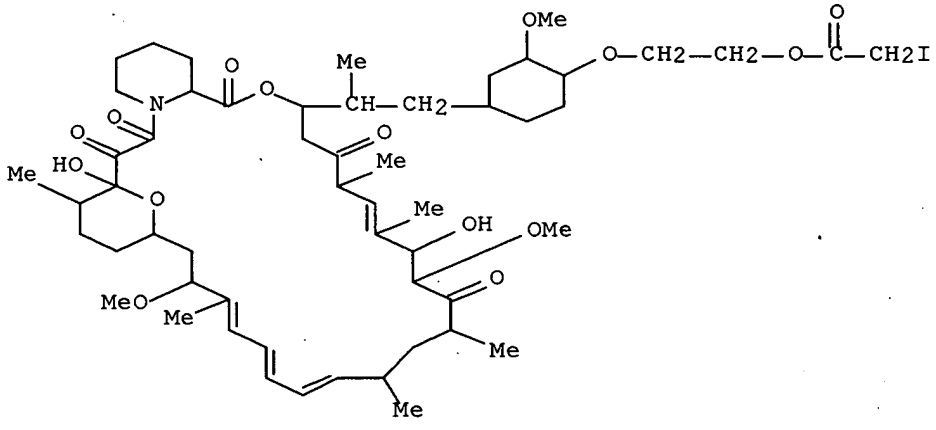


IT **326591-81-5P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and biol. activity of water soluble SDZ-RAD esters)

RN 326591-81-5 CAPLUS

CN Rapamycin, 42-O-[2-[(iodoacetyl)oxy]ethyl]- (9CI) (CA INDEX NAME)

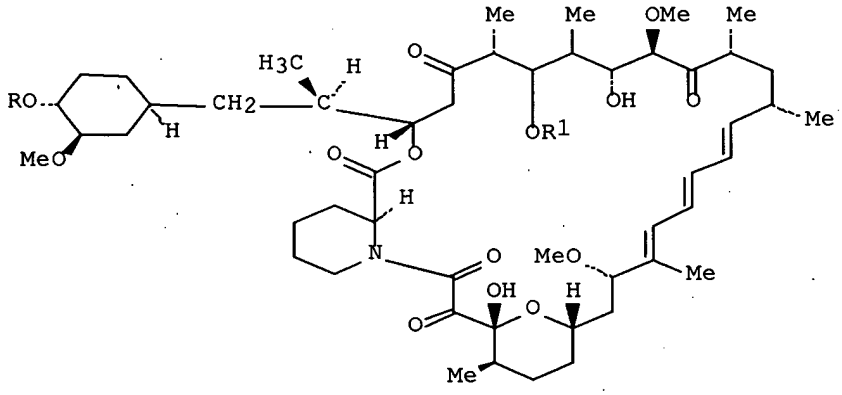


RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 19 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:439324 CAPLUS Full-text
DN 131:87755
TI synthesis and immunosuppressive activity of alkylated rapamycin derivatives
IN Hu, David Cheng; Greenfield, Alexander Aleksey; Caggiano, Thomas Joseph; Caufield, Craig Eugene
PA American Home Products Corporation, USA
SO U.S., 8 pp., Cont.-in-part of U.S. Ser. No. 926,251.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5922730	A	19990713	US 1998-103445	19980624
PRAI US 1996-25980P	P	19960909		
US 1997-926251	A2	19970905		

OS MARPAT 131:87755
GI



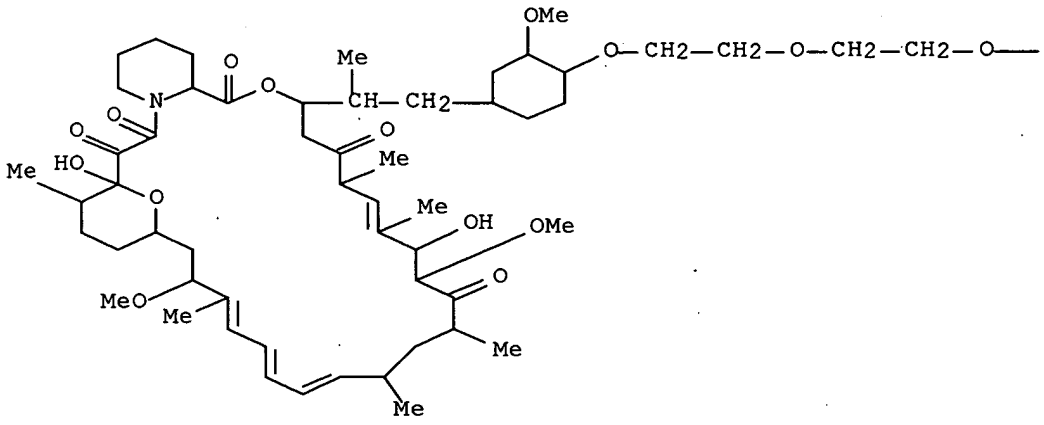
I

AB Synthesis of rapamycins (I) (R = haloalkyl, methoxyalkyl, H; R1 = arylalkyl, H, alkyl, alkenyl) which possess immunosuppressive and/or anti tumor and/or antiinflammatory activity in vivo and/or inhibit thymocyte proliferation in vitro is presented. I are useful in the treatment of transplantation rejection, autoimmune diseases such as lupus, rheumatoid arthritis, diabetes mellitus, multiple sclerosis and in the treatment of Candida albicans infections and also in treatment of diseases of inflammation.

IT **204633-78-3P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and immunosuppressive and antitumor activity of alkylated rapamycin derivs.)

RN 204633-78-3 CAPLUS
CN Rapamycin, 42-O-[2-[2-(2-methoxyethoxy)ethoxy]ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

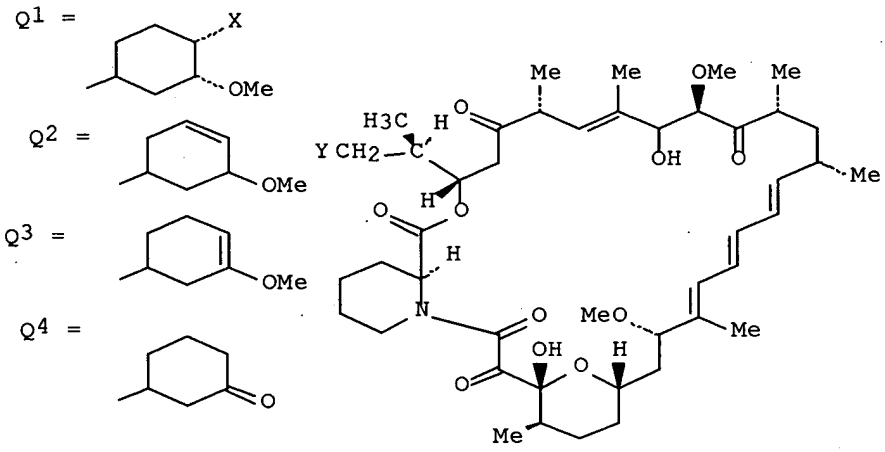
—CH2—CH2—OMe

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 20 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:175931 CAPLUS Full-text
DN 128:230188
TI synthesis and biological activity of rapamycin derivatives with unnatural stereochemistries
IN Grinfield, Alexander Alesksey; Hu, David Cheng; Caufield, Craig Eugene
PA American Home Products Corporation, USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9809972	A1	19980312	WO 1997-US15438	19970902
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9742461	A1	19980326	AU 1997-42461	19970902
PRAI	US 1996-709318	A	19960909		
	WO 1997-US15438	W	19970902		

OS MARPAT 128:230188
GI



I

AB Rapamycin derivs. (I) [Y = Q1, Q2, Q3, Q4; X = OH, -OR1, -SO2Ar, -SO2R1, N3, -OAr, -NH(C=O)Ar, -NH(C=O)R1, -NH(C=O)NR2R3, -NHCN, I, Cl, F, Br, -SCN, or 1,2,3-triazole optionally substituted with methoxycarbonyl; R1 = alkyl, cycloalkyl, (CH2)1-10NHR2, piperdinyl, pyrrolidinyl, piperazinyl, (CH2)1-10Ar, CH2CH(OR4)CH2OR5, CH2-1,2:3,4-diisopropylidenegalactose; R2, R3 = alkyl, Ar, H, (CH2)1-10Ar; R4, R5 = H, alkyl, (CH2)1-10Ar, together form isopropylidne; Ar = Ph, naphthyl, pyridyl, quinolyl, indolyl, imidazolyl, triazolyl, tetrazolyl, furanyl, and may be substituted with F, Cl, Br, I, NO2, OH, alkyl, alkoxy, CH2OH, 3,4-methylenedioxy] are prepared as well as pharmaceutically

acceptable salts when one can be formed. Is possess immunosuppressive and/or anti-tumor and/or antiinflammatory activity in vivo and/or inhibit thymocyte proliferation in vitro and are, therefore, useful in the treatment of transplantation rejection, autoimmune diseases such as lupus, rheumatoid arthritis, diabetes mellitus, multiple sclerosis and in the treatment of Candida albicans infections and also in treatment of diseases of inflammation..

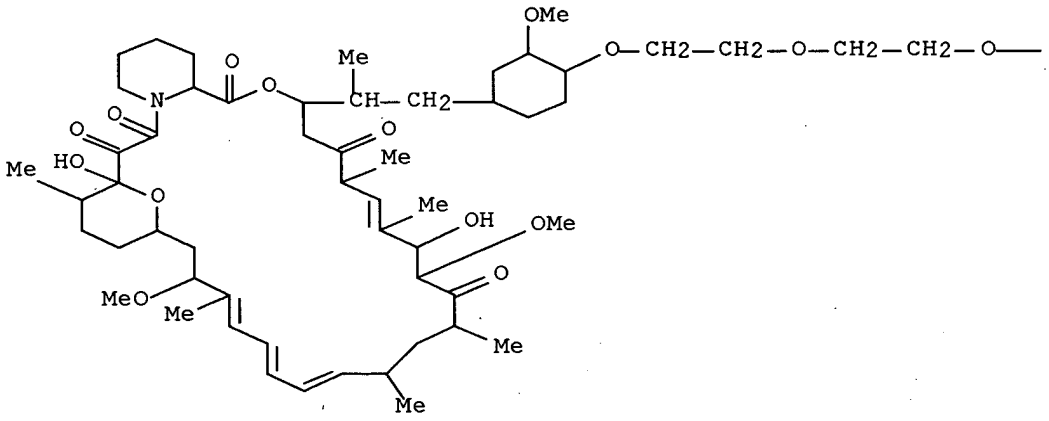
IT **204635-47-2P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and biol. activity of rapamycin derivs. with unnatural stereochemistries)

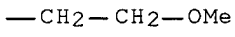
RN 204635-47-2 CAPLUS

CN Rapamycin, 42-O-[2-[2-(2-methoxyethoxy)ethoxy]ethyl]-, (42S)- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

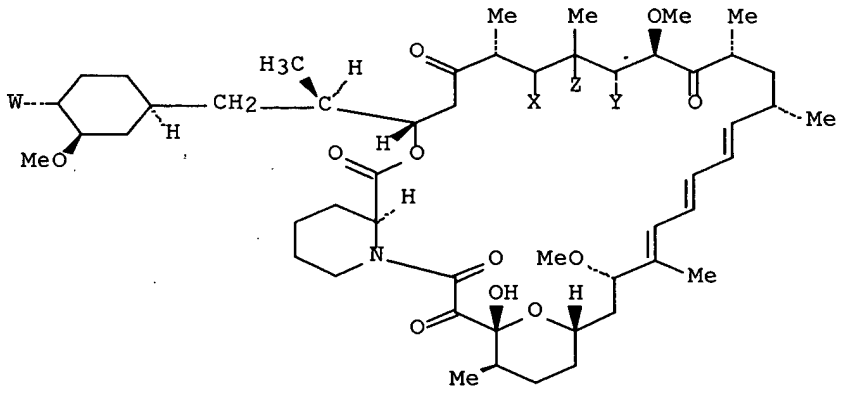


RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 21 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:175929 CAPLUS Full-text
DN 128:230187
TI synthesis and biological activity of alkylated rapamycin derivatives
IN Hu, David Cheng; Grinfield, Alexander Aleksey; Caggiano, Thomas Joseph; Caufield, Craig Eugene
PA American Home Products Corporation, USA
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9809970	A2	19980312	WO 1997-US15439	19970903
	WO 9809970	A3	19980416		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2266039	AA	19980312	CA 1997-2266039	19970903
	AU 9741768	A1	19980326	AU 1997-41768	19970903
	EP 927182	A2	19990707	EP 1997-939749	19970903
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
	CN 1235608	A	19991117	CN 1997-199423	19970903
	JP 2001500126	T2	20010109	JP 1998-512815	19970903
PRAI	US 1996-709591	A	19960909		
	WO 1997-US15439	W	19970903		

OS MARPAT 128:230187
GI



I

AB Rapamycin derivs. (I) [W, Y = OR1; X, Z together form a bond or W, X = OR2; Y, Z together form a bond; R1 = -(CH2)n-Ar (Ar is not Ph), -(CH2CH2O)nCH3 (n is not 1), -CH2CH2CH2O(CH2CH2O)m-CH3, -(CH2)n-CH2CH(OR3)CH2OR4; R3, R4 = H, alkyl, or R3, R4 together are ethylene, methylene or dimethylmethylene; -

CH2(CH2)n-OR3 (R3 is not H, alkyl, or C(O)alkyl); and -CH2(CH2)n-X where X is F, Cl, Br or I; R2 = H, alkyl, Ar(CH2)n-, alkenyl, -(CH2CH2O)nCH3, -CH2CH2CH2O(CH2CH2O)m-CH3, -CH2(CH2)n-OR3, -CH2(CH2)n-X where X is F, Cl, Br or I; and -(CH2)nCH2CH(OR5)CH2OR6 where R5 and R6 are selected independently from H, alkyl, -(CH2)n-Ar, -CONH(CH2)n-Ar or COC(CH3)2-(CH2)n-Ar, -COR7 and -CO2R7, where R7 is alkyl, alkenyl, or Ar; n = 1-10 independently; m = 1-5 independently; and Ar is selected independently from Ph, pyridinyl, quinolinyl, indolyl, furanyl; 1,2,3-triazolyl and tetrazolyl] are synthesized as well as pharmaceutically acceptable acid addition salt where one can be formed. Is possess immunosuppressive and/or anti tumor and/or antiinflammatory activity in vivo and/or inhibit thymocyte proliferation in vitro and are, therefore, useful in the treatment of transplantation rejection, autoimmune diseases such as lupus, rheumatoid arthritis, diabetes mellitus, multiple sclerosis and in the treatment of Candida albicans infections and also in treatment of diseases of inflammation..

IT **204633-78-3P**

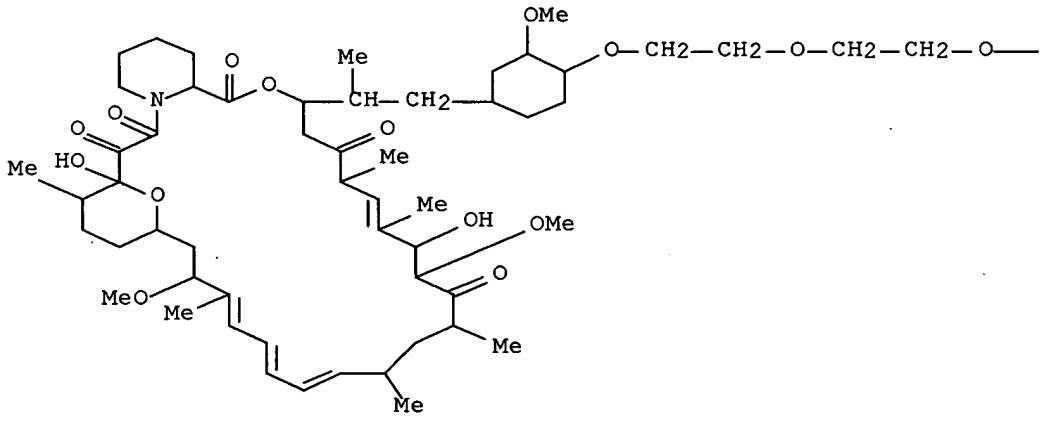
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis and biol. activity of alkylated rapamycin derivs.)

RN 204633-78-3 CAPLUS

CN Rapamycin, 42-O-[2-[2-(2-methoxyethoxy)ethoxy]ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



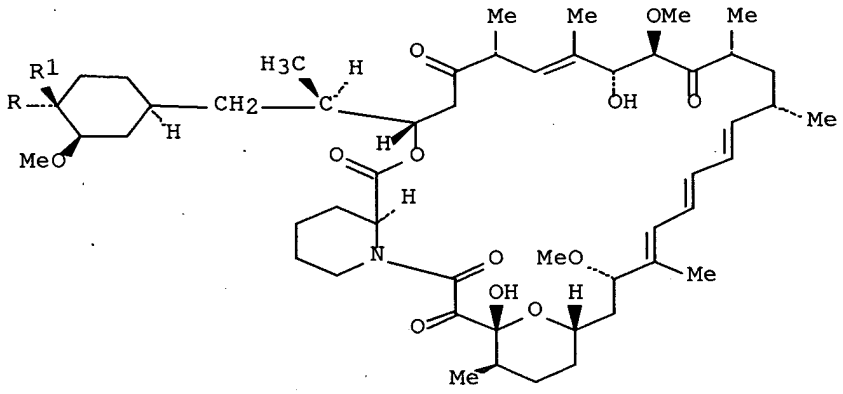
PAGE 1-B

—CH2—CH2—OMe

L6 ANSWER 22 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:425677 CAPLUS Full-text
DN 125:114399
TI Preparation of rapamycin derivatives as immunomodulators
IN Or, Yat S.; Luly, Jay R.; Wagner, Rolf
PA Abbott Laboratories, USA
SO U.S., 63 pp., Cont.-in-part of U.S. Ser. No. 155,064, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5527907	A	19960618	US 1994-327391	19941026
	CA 2175215	AA	19950526	CA 1994-2175215	19941107
	WO 9514023	A1	19950526	WO 1994-US12777	19941107
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 729471	A1	19960904	EP 1995-903106	19941107
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 09505299	T2	19970527	JP 1994-514482	19941107
	US 5583139	A	19961210	US 1995-423490	19950419
	US 5672605	A	19970930	US 1995-424931	19950419
PRAI	US 1993-155064	B2	19931119		
	US 1994-327391	A	19941026		
	WO 1994-US12777	W	19941107		

OS MARPAT 125:114399
GI



I

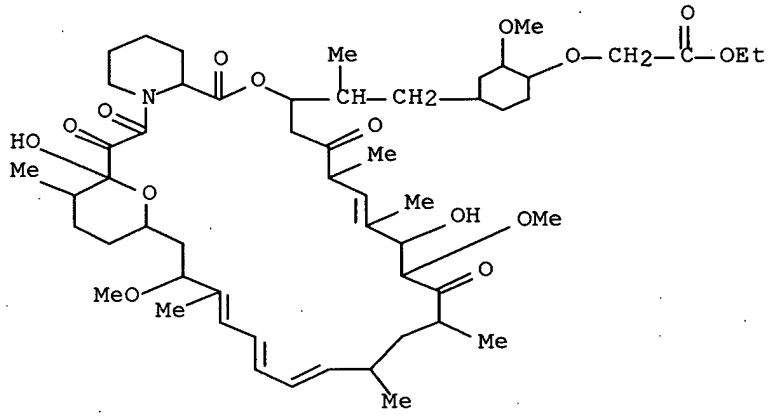
AB Title compds., such as I [R = FSO3, CF3SO3, morpholinocarbonyloxy, O2CNMeOMe, OCH2SMe, R1 = H; R = H, R1 = OH, 2-imidazolylthio, 1-methyl-2-imidazolylthio, N3, NH2, SH, 4-oxo-1,4-dihydro-1-pyridyl, 2-oxo-1,2-dihydro-1-pyridyl, OMe] were prepared from rapamycin. Thus, I [R = H, R1 = OH] was prepared by treating rapamycin with (FSO2)2O and hydrolyzing. This compound had an IC50 in the mixed leukocyte response test of 0.03 nM.

IT **151477-91-7P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of rapamycin derivs. as immunomodulators)

RN 151477-91-7 CAPLUS

CN Rapamycin, 42-O-(2-ethoxy-2-oxoethyl)- (9CI) (CA INDEX NAME)



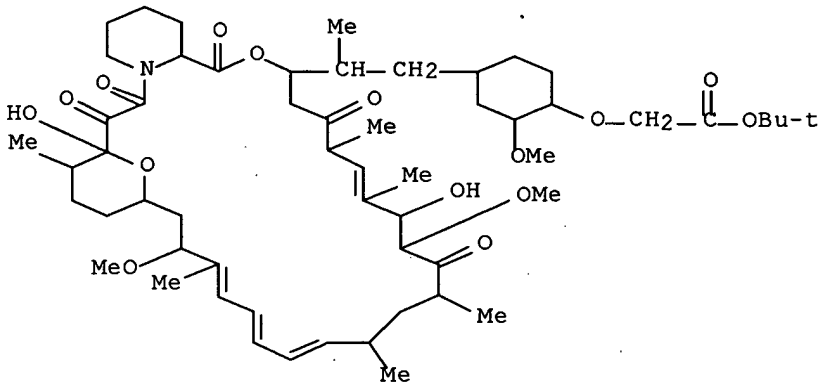
L6 ANSWER 23 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:994704 CAPLUS Full-text
DN 124:45690
TI Molecular cloning of cDNA for human effector proteins of rapamycin
IN Molnar-Kimber, Katherine Lu; Failli, Amedeo Arturo; Caggiano, Thomas Joseph; Nakanishi, Koji; Chen, Yanqiu
PA American Home Products Corp., USA; Trustees of Columbia University in the City of New York; Wyeth
SO Eur. Pat. Appl., 44 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 676471	A2	19951011	EP 1995-301475	19950307
	EP 676471	A3	19970820		
	EP 676471	B1	20040929		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	HU 72189	A2	19960328	HU 1995-673	19950306
	HU 218109	B	20000628		
	JP 08059696	A2	19960305	JP 1995-47408	19950307
	AT 278015	E	20041015	AT 1995-301475	19950307
	CA 2144223	AA	19950909	CA 1995-2144223	19950308
	AU 9513670	A1	19950914	AU 1995-13670	19950308
	ZA 9501931	A	19960909	ZA 1995-1931	19950308
	TW 404951	B	20000911	TW 1995-84102190	19950506
	AU 9917390	A1	19990520	AU 1999-17390	19990219
	AU 775722	B2	20040812	AU 2001-78263	20011008
PRAI	US 1994-207975	A	19940308		
	US 1994-312023	A	19940926		
	US 1995-384524	A	19950213		
	AU 1995-13670	A3	19950308		
	AU 1999-17390	A3	19990219		

AB Novel rapamycin effector proteins having mol. weight (SDS-PAGE) 210 kDa, 208 kDa, 148 kDa, and 125 kDa, resp., are identified from human leukemia cell line Molt 4 using a fusion protein of glutathione S-transferase-FK506 binding protein 12 (GST-FKBP) produced by Escherichia coli transformed with plasmid pGEX-FKBP. The 210-kDa protein is further isolated using the GST-FKBP12-rapamycin complex from BJAB cells and normal human T cells. The cDNA for 210-kDa protein is isolated and its amino acid sequence determined Therapeutic uses of the proteins as immunomodulatory agents, anti-restenosis or anti-tumor agents are claimed. Also claimed are the antisense RNA and antisense DNA of the cDNA.

IT **151477-92-8 171728-96-4**
RL: NUU (Other use, unclassified); USES (Uses)
(rapamycin analog; for isolation of human 210-kDa rapamycin effector protein binding to glutathione S-transferase-FK506 binding protein-rapamycin complex (RAPA-GST-FKBP))

RN 151477-92-8 CAPLUS
CN Rapamycin, 42-O-[2-(1,1-dimethylethoxy)-2-oxoethyl]- (9CI) (CA INDEX NAME)

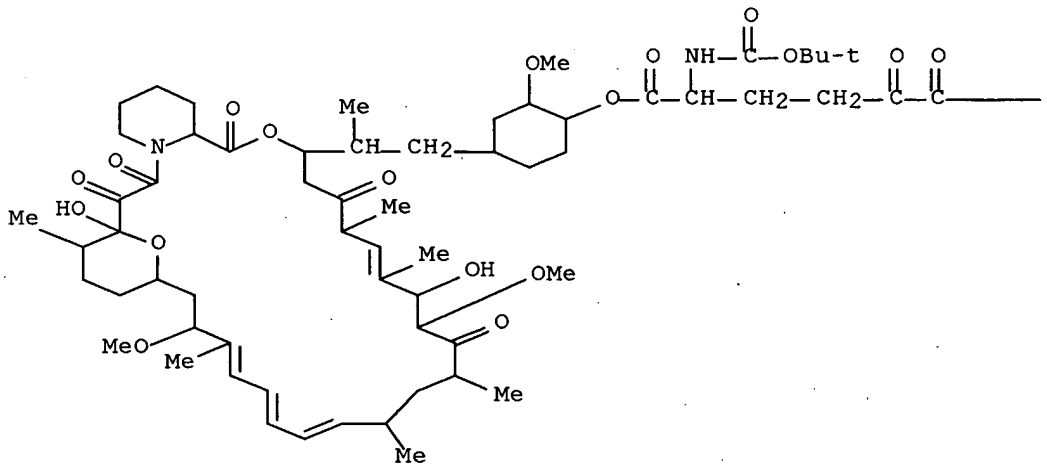


RN 171728-96-4 CAPLUS
CN Rapamycin, 42-[6-(1,1-dimethylethyl) 2-[[(1,1-dimethylethoxy)carbonyl]amino]-5-oxohexanedioate], compd. with ethyl acetate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 171728-95-3
CMF C66 H102 N2 O19

PAGE 1-A



PAGE 1-B

—OBu-t

CM 2

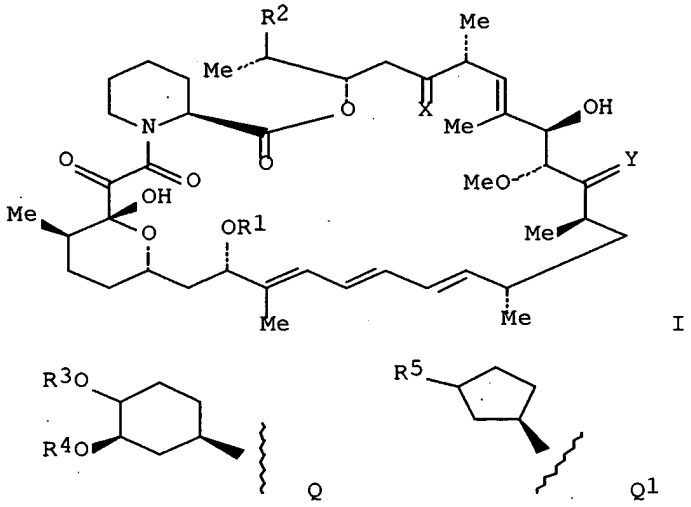
CRN 141-78-6
CMF C4 H8 O2

Et—O—Ac

L6 ANSWER 24 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:874738 CAPLUS Full-text
DN 123:285649
TI Rapamycin derivatives useful as immunosuppressants
IN Cottens, Sylvain; Sedrani, Richard
PA Sandoz Ltd., Switz.; Sandoz-Patent-GmbH; Sandoz-Erfindungen Verwaltungsgesellschaft m.b.H.
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9516691	A1	19950622	WO 1994-EP4191	19941216
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, US, UZ, VN				
	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2174731	AA	19950622	CA 1994-2174731	19941216
	AU 9512739	A1	19950703	AU 1995-12739	19941216
	AU 687491	B2	19980226		
	EP 734389	A1	19961002	EP 1995-903810	19941216
	EP 734389	B1	20000329		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	CN 1137797	A	19961211	CN 1994-194522	19941216
	CN 1046944	B	19991201		
	HU 74686	A2	19970128	HU 1996-1643	19941216
	BR 9408323	A	19970819	BR 1994-8323	19941216
	CZ 284650	B6	19990113	CZ 1996-1757	19941216
	AT 191218	E	20000415	AT 1995-903810	19941216
	ES 2146741	T3	20000816	ES 1995-903810	19941216
	PT 734389	T	20000929	PT 1995-903810	19941216
	FI 9602487	A	19960614	FI 1996-2487	19960614
	NO 9602540	A	19960614	NO 1996-2540	19960614
	US 5912253	A	19990615	US 1996-663169	19960614
	GR 3033545	T3	20000929	GR 2000-401237	20000531
PRAI	GB 1993-25800	A	19931217		
	GB 1993-25802	A	19931217		
	GB 1994-7138	A	19940411		
	GB 1994-21982	A	19941101		
	WO 1994-EP4191	W	19941216		

OS MARPAT 123:285649
GI



I

Q Q1

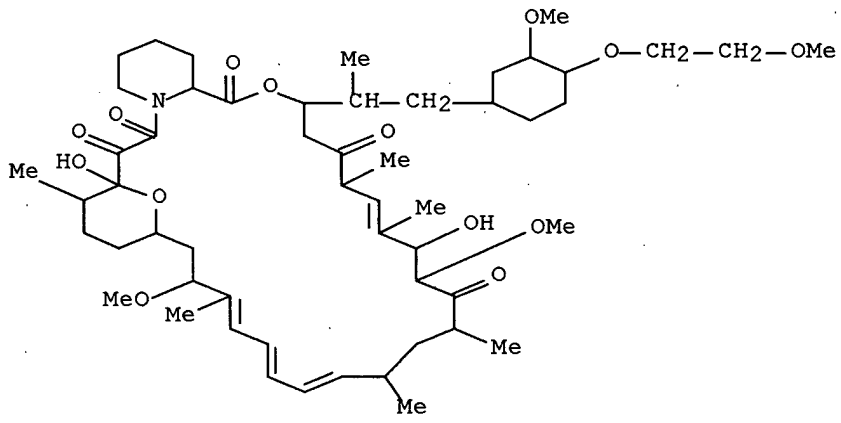
AB Novel demethoxy derivs. of rapamycin I [R1 = (un)substituted alkyl, alkylsilyl; R2 = Q, Q1; R3 = H, (un)substituted alkyl; R4 = H, Me; R3R4 = alkylene; R5 = acyl, hydroxymethyl, iminomethyl, methylenedioxy; X, Y = O, H,OR6; R6 = H, alkyl] were prepared as immunosuppressants (no data). Thus,rapamycin was treated with HOCH2C.tplbond.CEt to give 16-demethoxy-16-(2-pentyn-1-yloxy)rapamycin.

IT **169288-19-1**

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of alkoxydemethoxyrapamycins as immunosuppressants)

RN 169288-19-1 CAPLUS

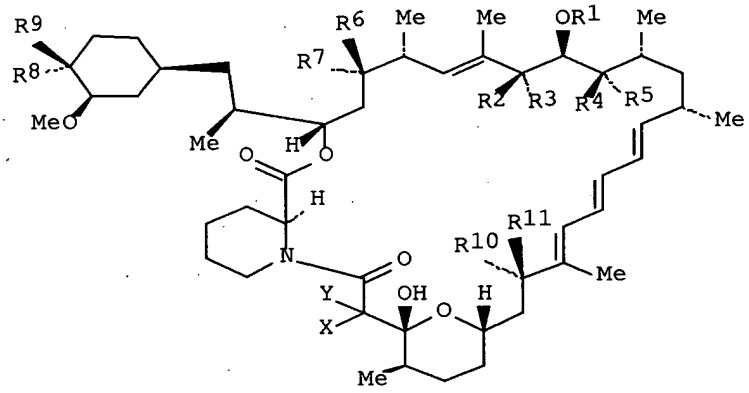
CN Rapamycin, 42-O-(2-methoxyethyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 25 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:861260 CAPLUS Full-text
DN 123:256433
TI Semisynthetic analogs of rapamycin (macrolides) as immunomodulators
IN Or, Yat Sun; Luly, Jay R.; Wagner, Rolf
PA Abbott Laboratories, USA
SO PCT Int. Appl., 203 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9514023	A1	19950526	WO 1994-US12777	19941107
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5527907	A	19960618	US 1994-327391	19941026
	EP 729471	A1	19960904	EP 1995-903106	19941107
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 09505299	T2	19970527	JP 1994-514482	19941107
PRAI	US 1993-155064	A	19931119		
	US 1994-327391	A	19941026		
	WO 1994-US12777	W	19941107		

OS MARPAT 123:256433
GI



I

AB Analogs of rapamycin I [R1 = H, alkyl, phenylalkyl, protective group; R2 = H, R3 = protected OH; R2R3 = O; R4, R6 = H, phenylalkyl, R5, R7 = OH, protected OH; R4, R6 = OH, protected OH, R5, R7 = H, phenylalkyl; R4R5 = O; R6R7 = O, N2, CH2, ketalized O, (un)substituted NOH; R8 = H, R9 = substituted OH; R10 = H, R11 = H, (un)substituted OH, SH; R10 = (un)substituted OH, SH, R11 = H; R10R11 = O; X = H, Y = OH, protected OH; X = OH, protected OH, Y = H; XY = O] were prepared Thus, rapamycin was treated with 4-O2NC6H4O2CCl to give the 42α-nitrophenyl carbonate which was treated with morpholine to give the morpholinecarboxylate I (R1 = Me, R2, R9 = H, R3 = OH, R4R5, R6R7, R10R11, XY = O, R8 = morpholinocarbonyloxy) (II). II had an IC50 in the rat mixed leukocyte response test of 0.13 nM.

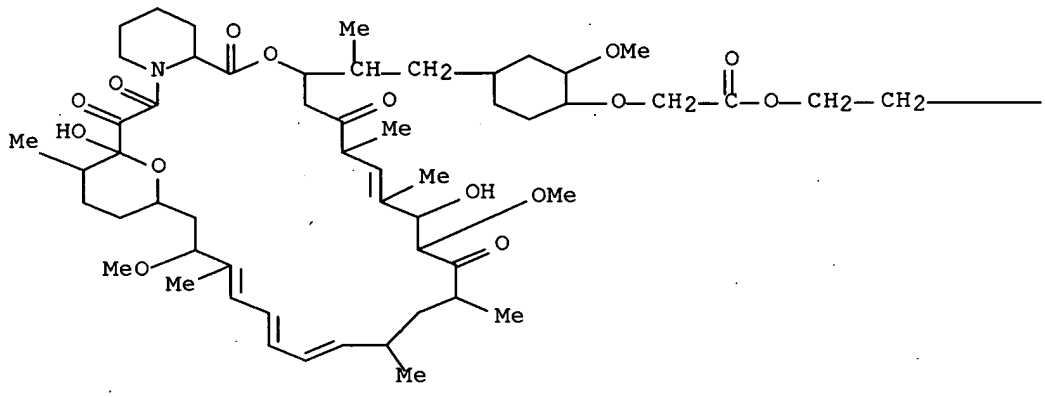
IT **169119-42-0P 169119-43-1P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(semisynthetic analogs of rapamycin as immunosuppressants)

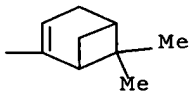
RN 169119-42-0 CAPLUS

CN Rapamycin, 42-O-[2-[2-(6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethoxy]-2-oxoethyl]-, [42(1R)]- (9CI) (CA INDEX NAME)

PAGE 1-A



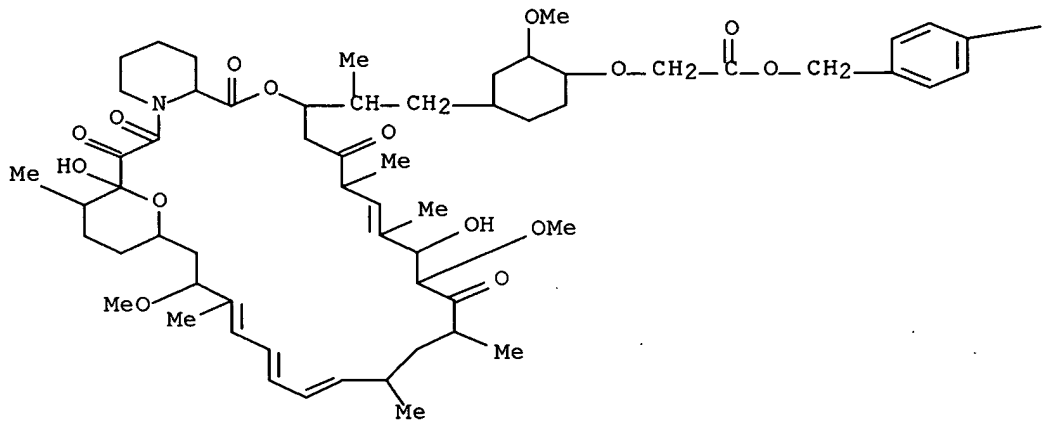
PAGE 1-B



RN 169119-43-1 CAPLUS

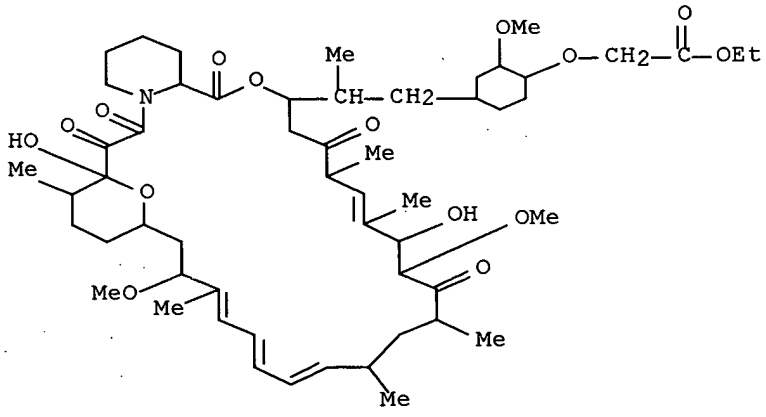
CN Rapamycin, 42-O-[2-[(4-nitrophenyl)methoxy]-2-oxoethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

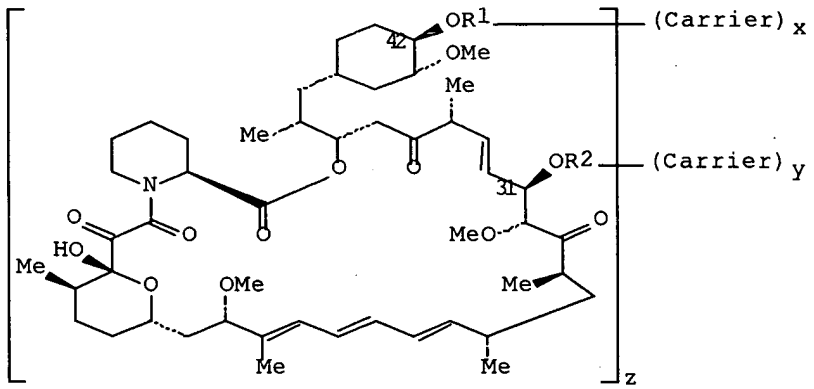
IT **151477-91-7P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(semisynthetic analogs of rapamycin as immunosuppressants)
RN 151477-91-7 CAPLUS
CN Rapamycin, 42-O-(2-ethoxy-2-oxoethyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 26 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:452026 CAPLUS Full-text
DN 122:213858
TI Preparation of rapamycin conjugates for generation of antibodies
IN Molnar-Kimber, Katherine Lu; Ocain, Timothy Donald; Caufield, Craig Eugene; Caggiano, Thomas Joseph; Failli, Amedeo Arturo
PA American Home Products Corp., USA
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9425072	A1	19941110	WO 1994-US4463	19940422
	W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9467119	A1	19941121	AU 1994-67119	19940422
	EP 1181938	A2	20020227	EP 2001-120777	19940422
	EP 1181938	A3	20020320		
	R: BE, CH, DE, ES, FR, GB, IT, LI				
	US 6328970	B1	20011211	US 2000-576952	20000524
	US 2001010920	A1	20010802	US 2001-773562	20010202
	US 6541612	B2	20030401		
	US 2002151088	A1	20021017	US 2002-124386	20020418
	JP 2004149542	A2	20040527	JP 2003-412072	20031210
	JP 2004168782	A2	20040617	JP 2003-412071	20031210
PRAI	US 1993-53030	A	19930423		
	US 1994-224207	A	19940414		
	US 1994-224205	A	19940414		
	EP 1994-915854	A3	19940422		
	JP 1994-524408	A3	19940422		
	WO 1994-US4463	W	19940422		
	US 1995-424983	B3	19950419		
	US 2000-576951	A3	20000524		
	US 2000-576952	A3	20000524		

OS MARPAT 122:213858
GI



I

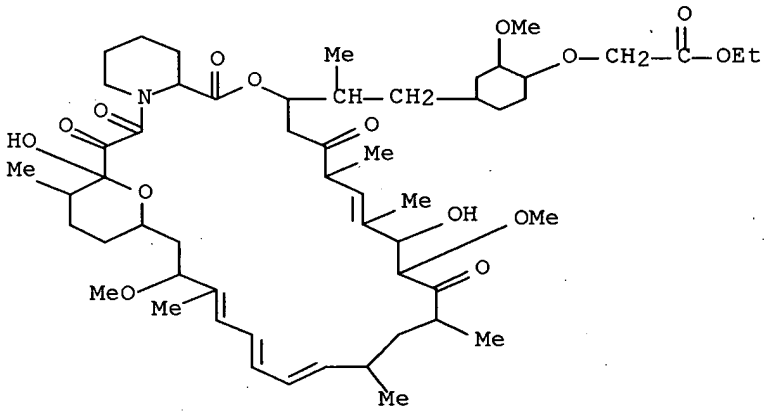
AB Title compds. I [(R1, R2 = H, (R3LR4) wherein L = linking group, R3 = CO, SO, SO2, PO2, POMe,CS, CH2CO; R4 = CO, NH, S, CH2, O; a = 1-5; z = 1-120), carrier = immunogenic material, detector material, solid matrix, salt; x, y = 0,1 with provisos], are prepared Succinic anhydride and dimethylaminopyridine were added to II to give II 42-ester with succinic acid which was treated with N-hydroxysuccinimide to give II 42-ester with N-hydroxysuccinimide hemisuccinate which was conjugated with proteins and horseradish peroxidase. Screening for monoclonal antibodies specific for II or its derivs. as well as immunoassay are given.

IT **151477-91-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of rapamycin conjugates for generation of antibodies)

RN 151477-91-7 CAPLUS

CN Rapamycin, 42-O-(2-ethoxy-2-oxoethyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 27 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:420799 CAPLUS Full-text
DN 123:32859
TI Aminoalkanoic esters of rapamycin
IN Failli, Amedeo A.; Steffan, Robert J.
PA American Home Products Co., USA
SO U.S., 11 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5389639	A	19950214	US 1993-174120	19931229
	CA 2179307	AA	19950706	CA 1994-2179307	19941228
	WO 9518133	A1	19950706	WO 1994-US14960	19941228
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN				
	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9515198	A1	19950717	AU 1995-15198	19941228
	EP 737197	A1	19961016	EP 1995-906728	19941228
	EP 737197	B1	20020508		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 09507236	T2	19970722	JP 1995-518187	19941228
	AT 217312	E	20020515	AT 1995-906728	19941228
	PT 737197	T	20020930	PT 1995-906728	19941228
	ES 2177627	T3	20021216	ES 1995-906728	19941228
	HK 1011355	A1	20020927	HK 1998-112279	19981124
PRAI	US 1993-174120	A	19931229		
	WO 1994-US14960	W	19941228		

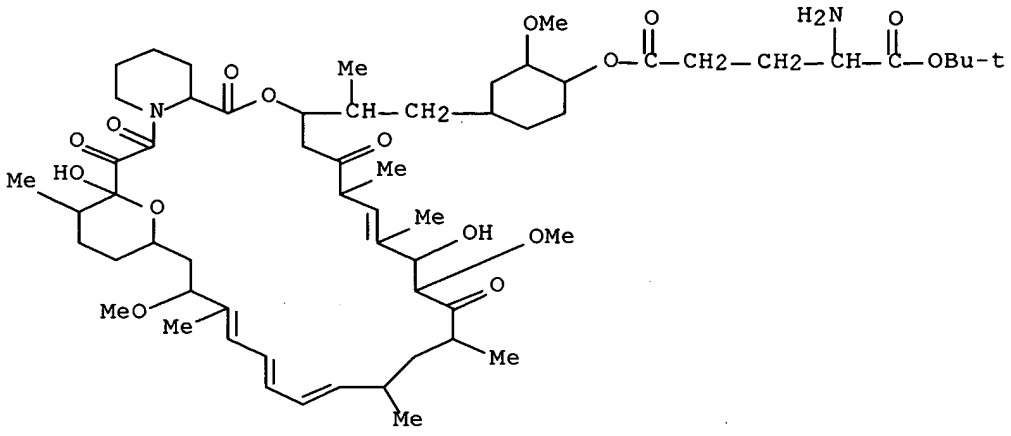
OS MARPAT 123:32859

AB 42- And/or 31-esters of rapamycin with aminoalkanoic acids were prepared for use as immunosuppressants. Thus, N-protected H-Glu-OCMe3 was treated with rapamycin, followed by deprotection to give the 42-ester of rapamycin with tert-Bu glutamate. This compound had an IC50 in the LAF lymphocyte proliferation test of 1.1 nm.

IT **163711-73-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of aminoalkanoic acid esters of rapamycin as immunosuppressants)

RN 163711-73-7 CAPLUS

CN L-Glutamic acid, 1-(1,1-dimethylethyl) ester, 5→42-ester with rapamycin (9CI) (CA INDEX NAME)

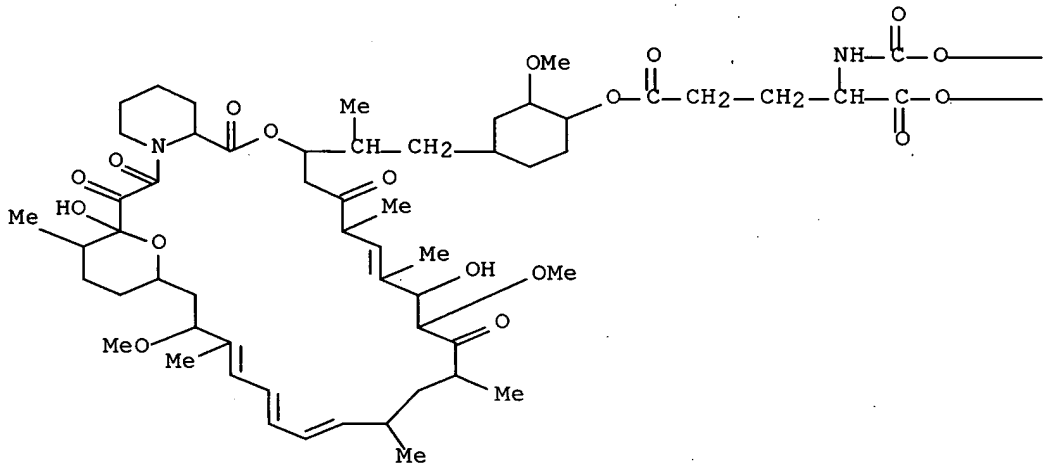


IT **163711-68-0P 163711-69-1P 163711-72-6P**
163877-47-2P 163877-49-4P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminoalkanoic acid esters of rapamycin as immunosuppressants)

RN 163711-68-0 CAPLUS

CN L-Glutamic acid, N-[(2-propenyloxy)carbonyl]-, 1-(phenylmethyl) ester, 5→42-ester with rapamycin (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

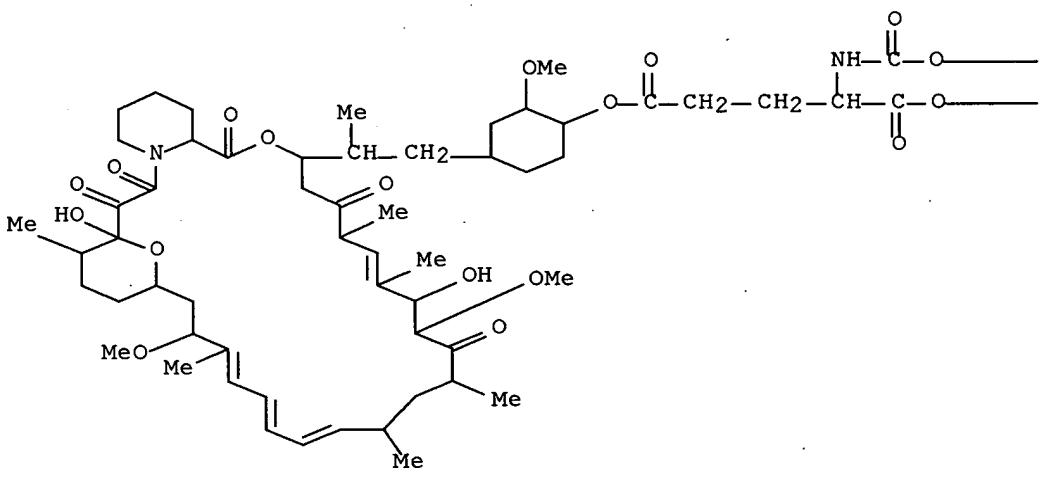
—CH_2—CH═CH_2

—CH_2—Ph

RN 163711-69-1 CAPLUS

CN L-Glutamic acid, N-[(phenylmethoxy)carbonyl]-, 1-(phenylmethyl) ester, 5→42-ester with rapamycin (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

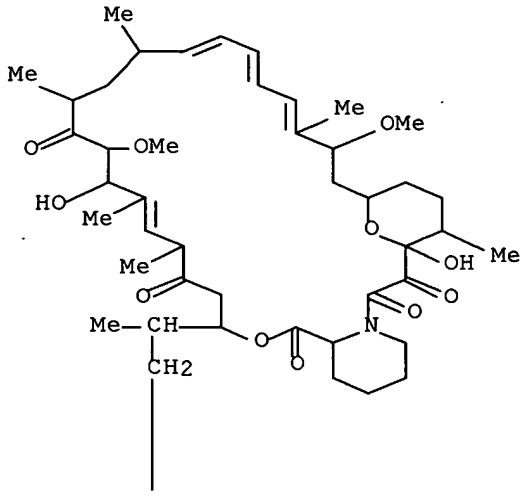
—CH_2—Ph

—CH_2—Ph

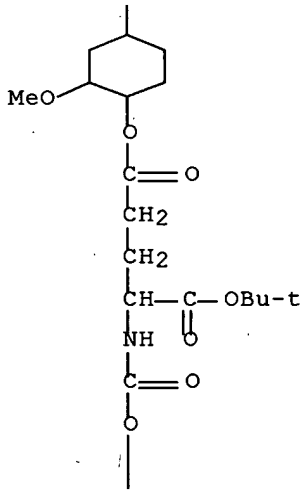
RN 163711-72-6 CAPLUS

CN L-Glutamic acid, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-, 1-(1,1-dimethylethyl) ester, 5→42-ester with rapamycin (9CI) (CA INDEX NAME)

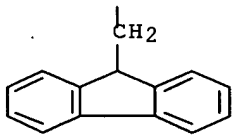
PAGE 1-A



PAGE 2-A

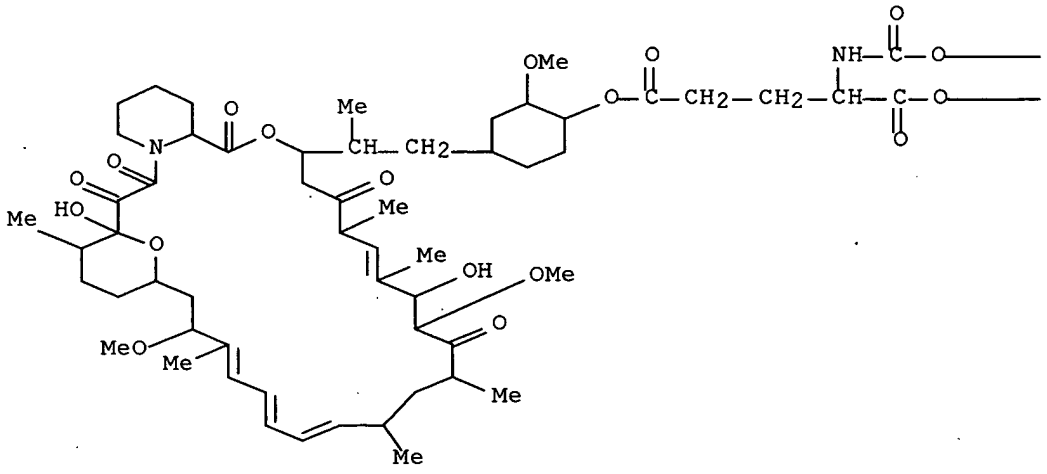


PAGE 3-A

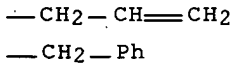


RN 163877-47-2 CAPLUS
CN D-Glutamic acid, N-[(2-propenyloxy)carbonyl]-, 1-(phenylmethyl) ester, 5→42-ester with rapamycin (9CI) (CA INDEX NAME)

PAGE 1-A

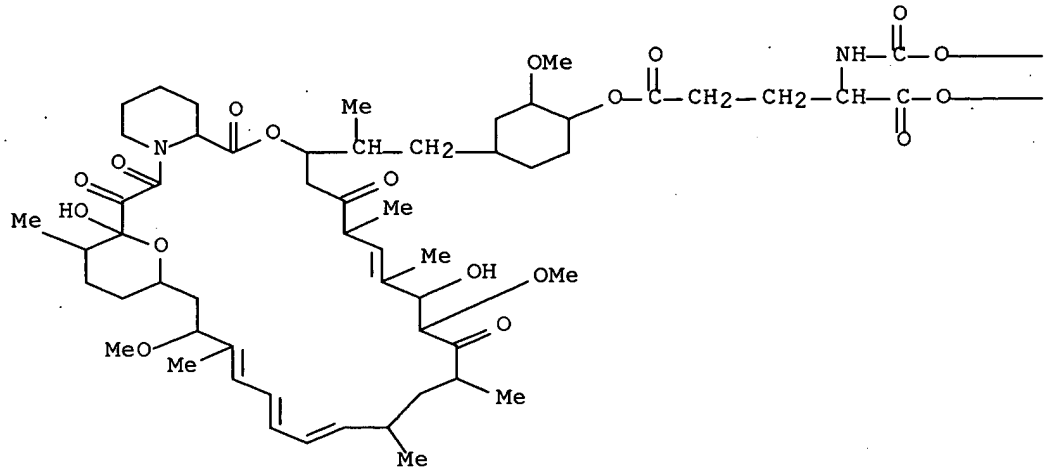


PAGE 1-B



RN 163877-49-4 CAPLUS
CN D-Glutamic acid, N-[(phenylmethoxy)carbonyl]-, 1-(phenylmethyl) ester, 5→42-ester with rapamycin (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

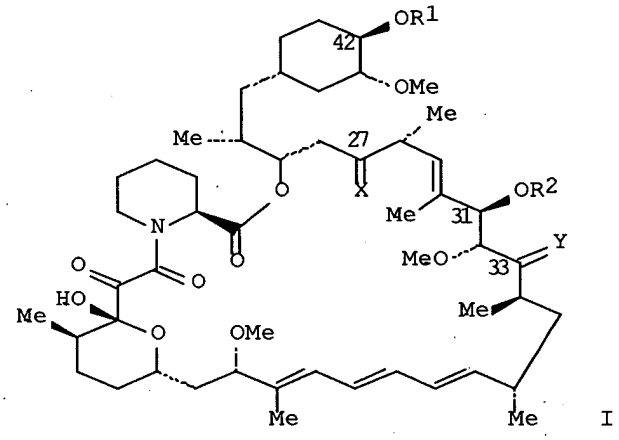
—CH_2—Ph

—CH_2—Ph

L6 ANSWER 28 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:331702 CAPLUS Full-text
DN 122:290589
TI Immunosuppressive rapamycin oximes and hydrazones
IN Kao, Wenling; Vogel, Robert L.; Abou-Gharbia, Magid A.; Caufield, Craig E.
PA American Home Products Corp., USA
SO U.S., 11 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5378836	A	19950103	US 1993-134224	19931008
PRAI US 1993-134224		19931008		

OS MARPAT 122:290589
GI



I

AB A compound of the structure I [wherein R1 and R2 are each, independently, e.g., hydrogen, CONHa{{(CR3R4)m(A(CR5R6)n)p}qB}r; SO2R7 ; SO3H; CHR8O(CH2)tR9; R3, R4, R5, R6, and B are each, independently, hydrogen, alkyl of 1-6 carbon atoms, alkenyl of 2-7 carbon atoms, alkynyl of 2-7 carbon atoms, hydroxyalkyl of 1-6 carbon atoms, alkoxyalkyl of 2-12 carbon atoms, alkylthioalkyl of 2-12 carbon atoms, alkylaminoalkyl of 2-12 carbon atoms, dialkylaminoalkyl of 3-12 carbon atoms, arylalkyl of 7-10 carbon atoms, cycloalkyl of 3-8 carbon atoms, OR10, SR10, halogen, CN, NO2, CF3, COR10, CO2R10, CONHR10, SO2R10, OSO3R10, NR10R11, NHCOR10, NHSO2R10, or Ar; X is :NOR12 or :NNR12R13 ; Y is O, :NOR12, or :NNR12R13; R7, R12, and R13 are each, independently, e.g., hydrogen, alkyl of 1-6 carbon atoms, alkenyl of 2-7 carbon atoms, alkynyl of 2-7 carbon atoms, arylalkyl of 7-10 carbon atoms, or Ar; R8, R9, R10, and R11 are each, independently, e.g., hydrogen, alkyl of 1-6 carbon atoms, arylalkyl of 7-10 carbon atoms; A is, e.g., CH2, O, S, SO, SO2; a=0-1; m=0-6; n=0-6; p=0-1; q=0-1; r=1-2; and t=1-4; proviso given]. I or a pharmaceutically acceptable salt thereof is useful as an immunosuppressive, antiinflammatory, antifungal, antiproliferative, and antitumor agent. Immunosuppressive activity for representative compds. of this invention was evaluated in an in vitro standard pharmacol. test procedure to measure lymphocyte proliferation (LAF) and in an

in vivo standard pharmacol. test procedure which evaluated the survival time of a pinch skin graft: LAF IC50 (nM) from 0.6 to > 1000; skin graft (days ± SD) from 7.0 ± 0.0 to 9.8 ± 0.4. at 4 mg/kg vs. 6-7 days for untreated control. Pharmaceutical formulations were given.

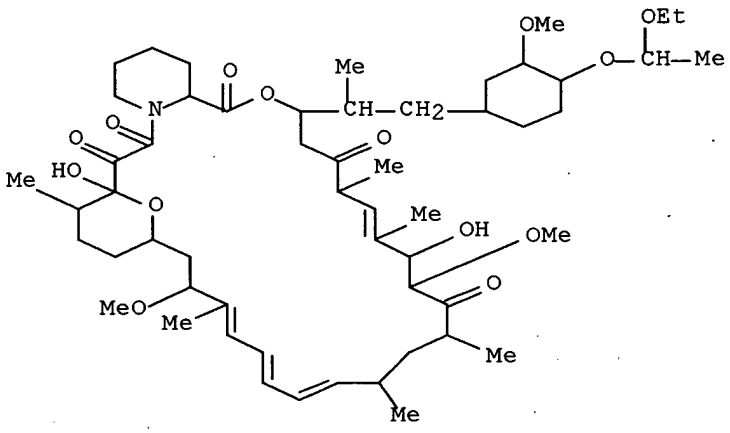
IT **162637-76-5P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(immunosuppressive rapamycin oximes and hydrazones)

RN 162637-76-5 CAPLUS

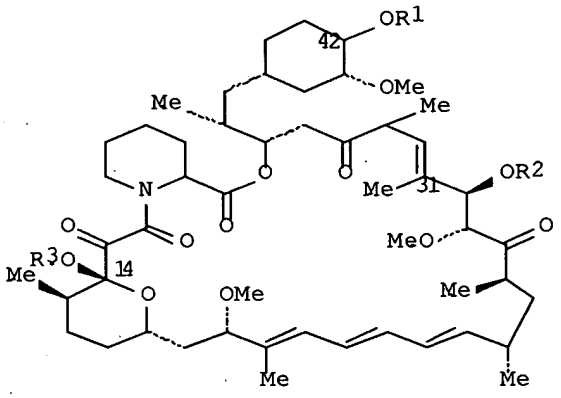
CN Rapamycin, 42-O-(1-ethoxyethyl)- (9CI) (CA INDEX NAME)



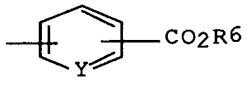
L6 ANSWER 29 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:331662 CAPLUS Full-text
DN 122:290588
TI Immunosuppressant and fungicidal rapamycin esters
IN Caufield, Craig E.
PA American Home Products Corp., USA
SO U.S., 11 pp. Cont.-in-part of U.S. Ser. No. 44,341.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5378696	A	19950103	US 1993-73857	19930608
	CA 2051781	AA	19920320	CA 1991-2051781	19910918
	US 5221670	A	19930622	US 1991-777983	19911017
	US 5358944	A	19941025	US 1993-44341	19930407
PRAI	US 1990-584833	B2	19900919		
	US 1991-777983	A1	19911017		
	US 1993-44341	A2	19930407		

OS MARPAT 122:290588
GI



I



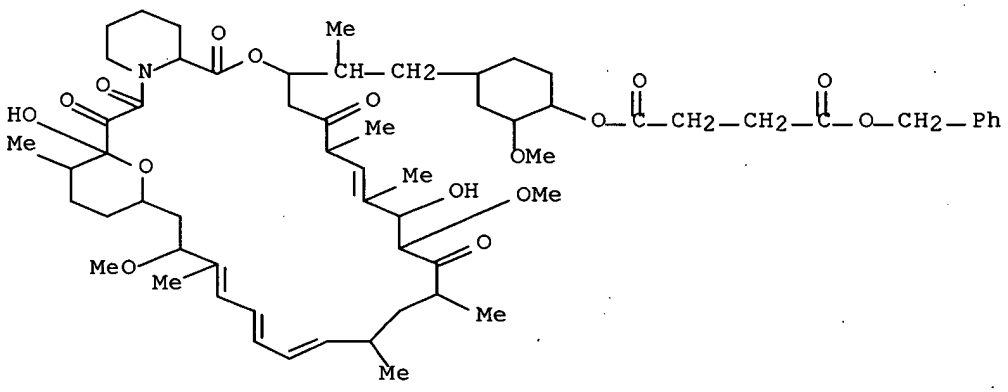
II

AB A compound of the structure I wherein R1, R2, and R3 are each, independently, hydrogen or COR4 with the proviso that R1, R2, and R3 are not all hydrogen; R4 is (CH2)mX(CH2)nCO2R5 or II; R5 and R6 are each, independently, hydrogen, alkyl, alkenyl, alkynyl, (CH2)pNR9R10, mono-, di-, or tri-hydroxyalkyl, aralkyl, or aryl; CR7R8, O, or S; R7, R8, R9, and R10 are each, independently, hydrogen or alkyl; Y is CH or N: m is 0-4; n is 0-4; p is 0-4; with the proviso that m and n are not both 0 when X is O or S; or a pharmaceutically acceptable salt thereof, which is by virtue of its immunosuppressive activity is useful in treating transplantation rejection, host vs. graft disease, autoimmune diseases, and diseases of inflammation, by virtue of its antitumor activity useful in treating tumors, and by virtue of its antifungal activity is useful in treating fungal infections. Immunosuppressive activity was evaluated in an in vitro standard pharmacol. test procedure to measure lymphocyte proliferation (LAF) and in two in vivo standard pharmacol. test procedures: the popliteal lymph node (PLN) test procedure which measured the

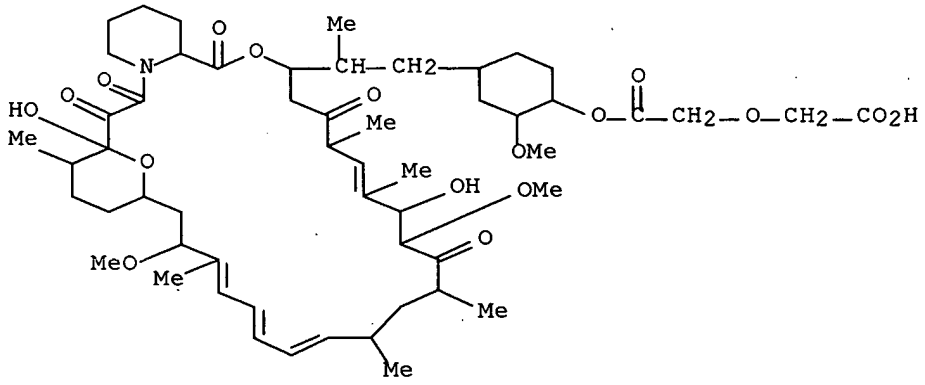
effect of compds. of this invention on a mixed lymphocyte reaction and the second in vivo procedure evaluated the survival time of a pinch skin graft. In the in vitro test screening, up to 97% inhibition of lymphoproliferation was observed for rapamycin 42-monomethylsuccinate at 100 nM; for the PLN test, pos. ratios of up to 2.08 were observed; skin graft (days ± SD) of 7.8 ± 1.7 to 12.7 ± 0.9 were observed Antifungal activity of the compds. of this invention was measured against 5 strains of Candida albicans: MIC (μg/mL) of 0.1 to > 0.4, indicating the compds. are less active than parent rapamycin. Pharmaceutical formulations were given.

IT **143136-12-3P 143136-14-5P 155589-15-4P**
162884-13-1P 162884-14-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(immunosuppressant and fungicidal rapamycin esters)

RN 143136-12-3 CAPLUS
CN Rapamycin, 42-(phenylmethyl butanedioate) (9CI) (CA INDEX NAME)



RN 143136-14-5 CAPLUS
CN Rapamycin, 42-[(carboxymethoxy)acetate] (9CI) (CA INDEX NAME)

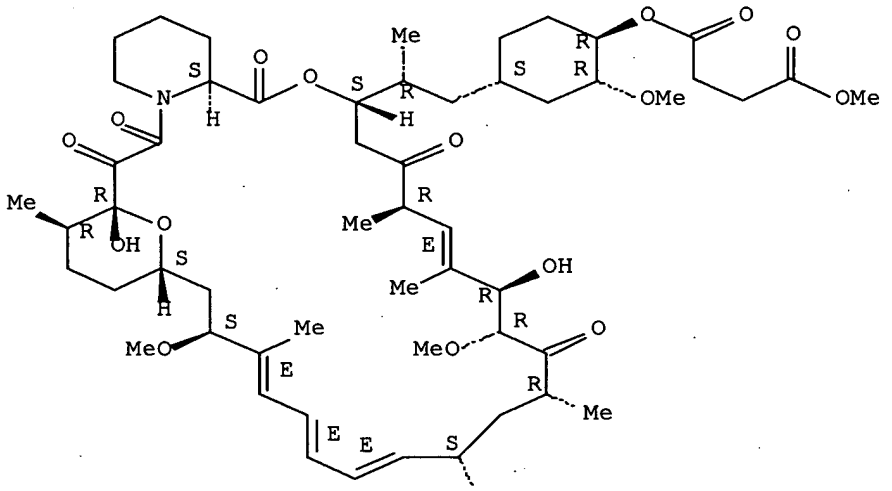


RN 155589-15-4 CAPLUS

CN Rapamycin, 42-(methyl butanedioate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

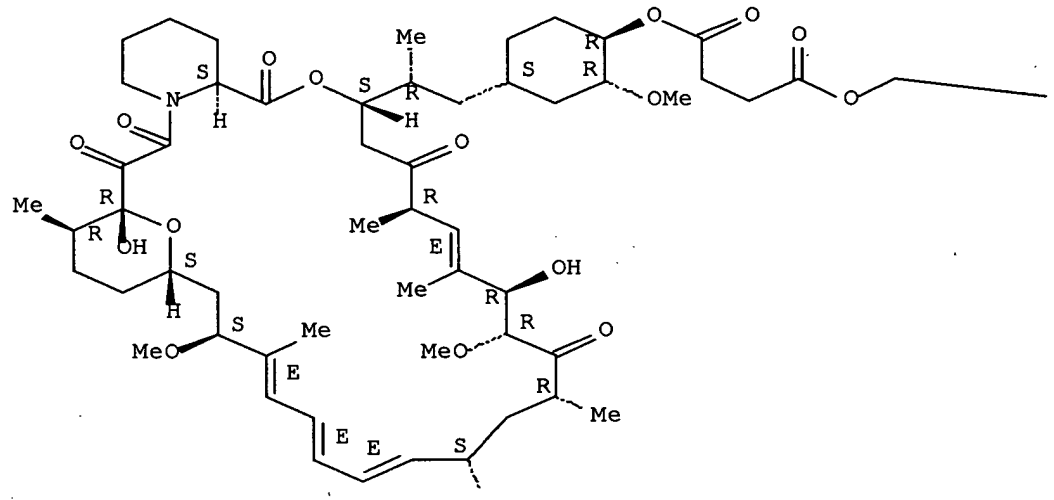


PAGE 2-A

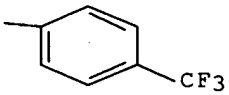
RN 162884-13-1 CAPLUS
CN Rapamycin, 42-[[4-(trifluoromethyl)phenyl]methyl butanedioate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

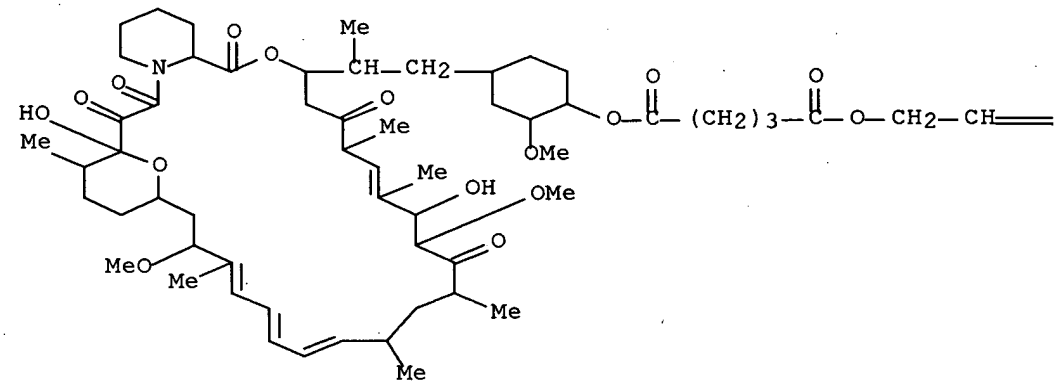


PAGE 2-A

Me

RN 162884-14-2 CAPLUS
CN Rapamycin, 42-(2-propenyl pentanedioate) (9CI) (CA INDEX NAME)

PAGE 1-A



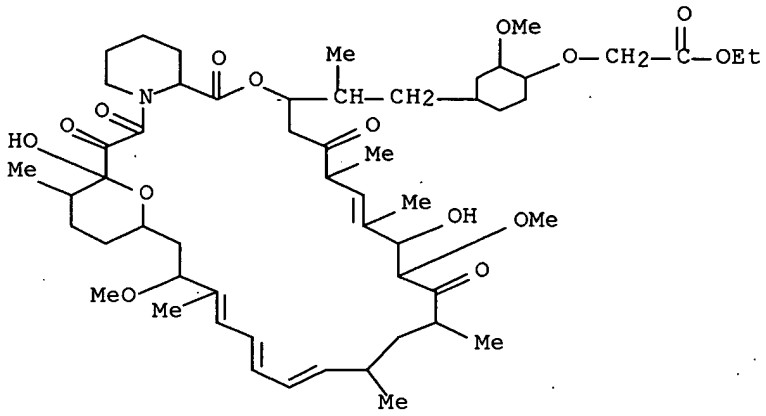
PAGE 1-B

$=CH_2$

L6 ANSWER 30 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:314312 CAPLUS Full-text
DN 122:123081
TI Rapamycin conjugates and antibodies
IN Gonzalez, Eduardo; Russell, John C.; Molnar-Kimber, Katherine L.
PA Abbott Laboratories, USA
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9425022	A1	19941110	WO 1994-US4434	19940422
	W: AU, CA, JP, KR				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2161101	AA	19941110	CA 1994-2161101	19940422
	AU 9467720	A1	19941121	AU 1994-67720	19940422
	AU 686629	B2	19980212		
	EP 710110	A1	19960508	EP 1994-915854	19940422
	EP 710110	B1	20020306		
	R: BE, CH, DE, ES, FR, GB, IT, LI				
	JP 08509499	T2	19961008	JP 1994-524408	19940422
	EP 1181938	A2	20020227	EP 2001-120777	19940422
	EP 1181938	A3	20020320		
	R: BE, CH, DE, ES, FR, GB, IT, LI				
	ES 2176245	T3	20021201	ES 1994-915854	19940422
	US 6328970	B1	20011211	US 2000-576952	20000524
	US 2001010920	A1	20010802	US 2001-773562	20010202
	US 6541612	B2	20030401		
	US 2002151088	A1	20021017	US 2002-124386	20020418
	JP 2004149542	A2	20040527	JP 2003-412072	20031210
	JP 2004168782	A2	20040617	JP 2003-412071	20031210
PRAI	US 1993-53030	A	19930423		
	US 1994-224205	A	19940414		
	EP 1994-915854	A3	19940422		
	JP 1994-524408	A3	19940422		
	WO 1994-US4434	W	19940422		
	US 1995-424983	B3	19950419		
	US 2000-576951	A3	20000524		
	US 2000-576952	A3	20000524		

OS MARPAT 122:123081
AB An immunoassay method for determination of rapamycin in blood comprises the use of rapamycin or secorapamycin 42-ester conjugates with fluorescein derivs. as immunogenic mols. for the generation of antibodies specific for rapamycin. Rapamycin 42-ester with succinic acid (100 mg) reacted overnight with 12 mg of N-hydroxysuccinimide to obtain rapamycin 42-ester with N-hydroxysuccinimide hemisuccinate (I). To 4.2 mg of 5- glycinylfluoresceinamide, 4 mg of I was added and after reaction for 2 h the conjugate obtained was purified by TLC.
IT **151477-91-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(rapamycin ester conjugates with fluorescein derivs. for immunoassay of rapamycin in blood)
RN 151477-91-7 CAPLUS
CN Rapamycin, 42-O-(2-ethoxy-2-oxoethyl)- (9CI) (CA INDEX NAME)


OMe
O
Me
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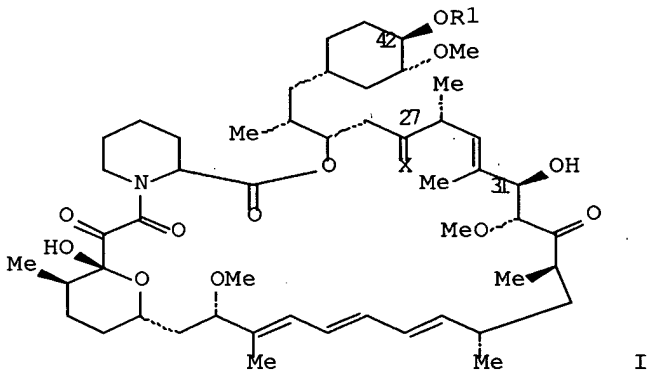
O—CH2—C—OEt
N
O
CH—CH2
O
HO
O
Me
Me
O
Me
OH
OMe
O
MeO
Me
Me
Me

L6 ANSWER 31 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:305782 CAPLUS Full-text
DN 122:187267
TI Immunosuppressive rapamycin oximes
IN Failli, Amedeo A.; Steffan, Robert J.; Caufield, Craig E.; Hu, David C.; Grinfeld, Alexander A.
PA American Home Products Corporation, USA
SO U.S., 10 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5373014	A	19941213	US 1993-134237	19931008
	US 5446048	A	19950829	US 1994-309816	19940921
PRAI	US 1993-134237	A3	19931008		

OS MARPAT 122:187267
GI



I

AB A compound of the structure I wherein R1 CO(CH2)a(Y)b(CH2)cCO2R2, CO(CH2)dCH(NHR3)R4, CO(CH2)eNR5R6, or CO2R7; R2 is hydrogen, alkyl, alkenyl, alkynyl, trifluoromethyl, arylalkyl, or Ar; R3 is hydrogen, alkyl, alkenyl, alkynyl, trifluoromethyl, arylalkyl, or CO2R8; R4 is alkyl, alkenyl, alkynyl, trifluoromethyl, arylalkyl, Ar, aminoalkyl, thioalkyl, alkylthioalkyl, hydroxyalkyl, or CO2R8; R5 is hydrogen, alkyl, alkenyl, alkynyl, trifluoromethyl, arylalkyl, Ar, or CO2R8; R6 is hydrogen, alkyl, alkenyl, alkynyl, trifluoromethyl, arylalkyl, or Ar; R7 is alkyl, alkenyl, alkynyl, trifluoromethyl, arylalkyl, or Ar; R8 is hydrogen, alkyl, alkenyl, alkynyl, trifluoromethyl, arylalkyl, fluorenylmethyl, or Ar; Y is O or S; X is :NO(CH2)fZ or :NOAr; Z is hydrogen, alkenyl, alkynyl, alkoxy, cyano, fluoro, trifluoromethyl, NR5 R6, aryloxy, or Ar; Ar is aryl which may be optionally mono-, di-, or tri- substituted; a=0-4; b=0-1; c=0-4; d=0-6; e=0-6; and f=0-6; or a pharmaceutically acceptable salt thereof, with the proviso that when f is 0, Z is hydrogen and further provided that when R3 or R5 is CO2R8, R8 is not hydrogen which is useful as an immunosuppressive, antiinflammatory, antifungal, antiproliferative, and antitumor agent. Evaluation of immunosuppressive activity: in-vitro comitogen-induced thymocyte proliferation IC50 (nM) from 4.1 to 432; in vivo survival time of pinch skin graft of 10.0 ±

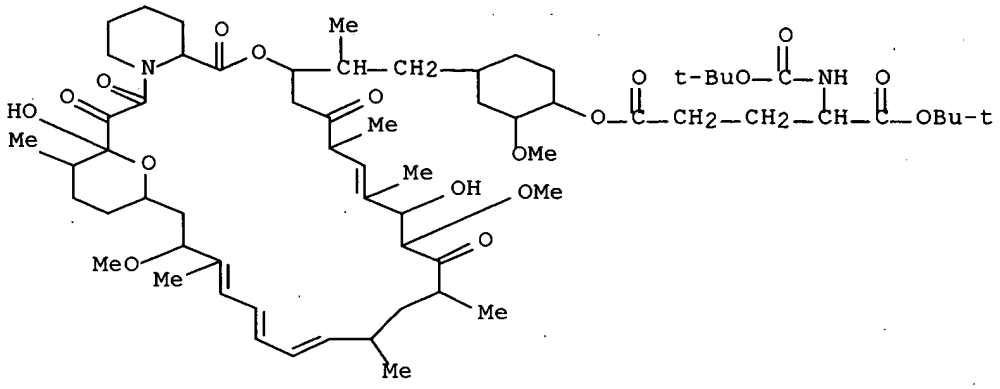
0.2 and 11.2 ± 0.8 days at 4 mg/kg vs. 6-7 days for untreated control. Pharmaceutical formulations were given.

IT **143136-06-5**

RL: RCT (Reactant); RACT (Reactant or reagent)
(immunosuppressive rapamycin oximes)

RN 143136-06-5 CAPLUS

CN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-, 1-(1,1-dimethylethyl) ester, 42-ester with rapamycin (9CI) (CA INDEX NAME)



L6 ANSWER 32 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:283340 CAPLUS Full-text
DN 122:54000
TI Monoclonal antibody to rapamycin for immunoassay
IN Quesniaux, Valerie; Sedrani, Richard
PA Sandoz-Erfindungen Verwaltungsgesellschaft mbH, Austria; Sandoz-Patent-G.m.b.H.; Sandoz Ltd.
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

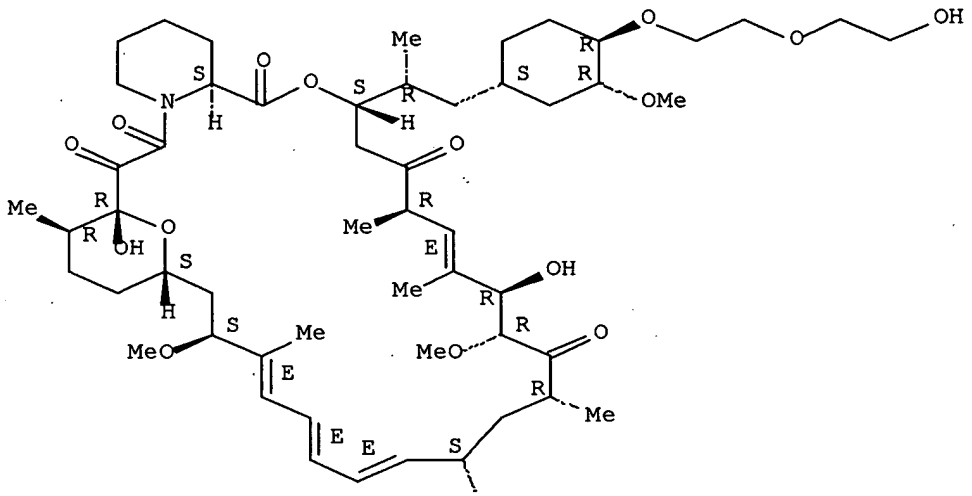
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9424304	A1	19941027	WO 1994-EP1006	19940330
	W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TT, UA, US, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2156397	AA	19941027	CA 1994-2156397	19940330
	AU 9465377	A1	19941108	AU 1994-65377	19940330
	AU 677321	B2	19970417		
	EP 693132	A1	19960124	EP 1994-913093	19940330
	EP 693132	B1	19971217		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	BR 9406210	A	19960206	BR 1994-6210	19940330
	CN 1120854	A	19960417	CN 1994-191718	19940330
	CN 1080312	B	20020306		
	HU 72835	A2	19960528	HU 1995-1975	19940330
	HU 221606	B	20021128		
	JP 08508647	T2	19960917	JP 1994-522682	19940330
	JP 3397325	B2	20030414		
	AT 161289	E	19980115	AT 1994-913093	19940330
	ES 2110230	T3	19980201	ES 1994-913093	19940330
	CZ 284431	B6	19981111	CZ 1995-2583	19940330
	SK 280048	B6	19990712	SK 1995-1257	19940330
	JP 2001302698	A2	20011031	JP 2001-78335	19940330
	RU 2175672	C2	20011110	RU 1995-119595	19940330
	JP 2003024065	A2	20030128	JP 2002-130451	19940330
	PL 185855	B1	20030829	PL 1994-310967	19940330
	FI 9504319	A	19950914	FI 1995-4319	19950914
	FI 110670	B1	20030314		
	NO 9503975	A	19951124	NO 1995-3975	19951006
	US 2002022717	A1	20020221	US 2001-757212	20010109
	US 6635745	B2	20031021		
	US 2002002273	A1	20020103	US 2001-933104	20010820
PRAI	GB 1993-7491	A	19930408		
	JP 1994-522682	A3	19940330		
	WO 1994-EP1006	W	19940330		
	US 1995-532837	B1	19951005		
	US 1998-72278	B1	19980504		
	US 2000-585743	A3	20000602		

AB Monoclonal antibodies to rapamycin and to 40-O-alkylated derivs. of rapamycin are provided, together with nobel haptens, immunogenic conjugates, and processes for making them and assay kits for using them. In example, 40-O- and 28-O-activated rapamycin derivs. and their immunogenic conjugates with keyhole limpet hemocyanin or ovalbumin or albumin were prepared for monoclonal antibody production for use in ELISA of rapamycin.
IT **159351-77-6**

RL: ANT (Analyte); MSC (Miscellaneous); ANST (Analytical study)(preparation of rapamycin conjugates and monoclonal antibody to rapamycin for ELISA)
RN 159351-77-6 CAPLUS
CN Rapamycin, 42-O-[2-(2-hydroxyethoxy)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

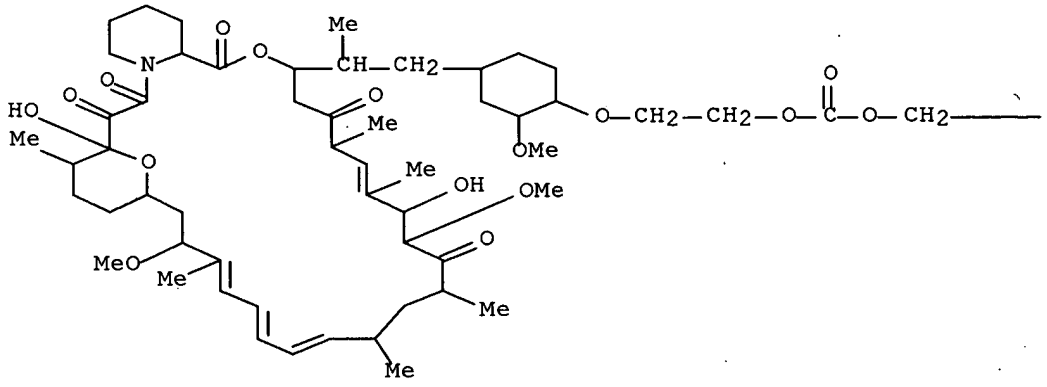
PAGE 1-A



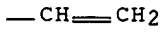
PAGE 2-A

IT **160091-38-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)(preparation of rapamycin conjugates and monoclonal antibody to rapamycin for ELISA)
RN 160091-38-3 CAPLUS
CN Rapamycin, 42-O-[2-[[(2-propenyloxy)carbonyl]oxy]ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



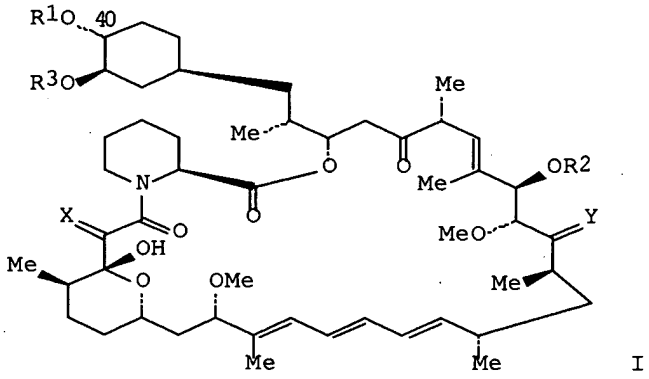
PAGE 1-B



L6 ANSWER 33 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:220179 CAPLUS Full-text
DN 122:9774
TI O-alkylated rapamycin derivatives and their use, particularly as immunosuppressants
IN Cottens, Sylvain; Sedrani, Richard
PA Sandoz-Erfindungen Verwaltungsgesellschaft M.B.H., Austria; Sandoz-Patent-GmbH; Sandoz Ltd.
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9409010	A1	19940428	WO 1993-EP2604	19930924
	W: AU, CA, CZ, FI, HU, JP, KR, NO, NZ, PL, RO, RU, SK, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2145383	AA	19940428	CA 1993-2145383	19930924
	CA 2145383	C	20041116		
	CA 2476257	AA	19940428	CA 1993-2476257	19930924
	AU 9348192	A1	19940509	AU 1993-48192	19930924
	AU 676198	B2	19970306		
	EP 663916	A1	19950726	EP 1993-920822	19930924
	EP 663916	B1	19981125		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	HU 71232	A2	19951128	HU 1995-1016	19930924
	JP 08502266	T2	19960312	JP 1994-509552	19930924
	JP 3117462	B2	20001211		
	CZ 283333	B6	19980218	CZ 1995-899	19930924
	AT 173736	E	19981215	AT 1993-920822	19930924
	ES 2124793	T3	19990216	ES 1993-920822	19930924
	PL 176174	B1	19990430	PL 1993-308268	19930924
	RO 114451	B1	19990430	RO 1995-686	19930924
	RU 2143434	C1	19991227	RU 1995-110053	19930924
	EP 1413581	A1	20040428	EP 2003-28783	19930924
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
	AT 272063	E	20040815	AT 1997-114343	19930924
	ES 2225919	T3	20050316	ES 1997-114343	19930924
	NO 9501312	A	19950608	NO 1995-1312	19950405
	NO 307053	B1	20000131		
	FI 9501678	A	19950407	FI 1995-1678	19950407
	FI 109540	B1	20020830		
	US 5665772	A	19970909	US 1995-416673	19950407
	US 6440990	B1	20020827	US 1997-862911	19970523
	EP 867438	A1	19980930	EP 1997-114343	19970903
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
	JP 11240884	A2	19990907	JP 1998-308355	19981029
	JP 3568800	B2	20040922		
	FI 2000001943	A	20000904	FI 2000-1943	20000904
PRAI	GB 1992-21220	A	19921009		
	CA 1993-2145383	A3	19930924		
	EP 1993-920822	A3	19930924		
	WO 1993-EP2604	W	19930924		
	US 1995-416673	A3	19950407		
	EP 1997-114343	A3	19970903		

OS MARPAT 122:9774
GI



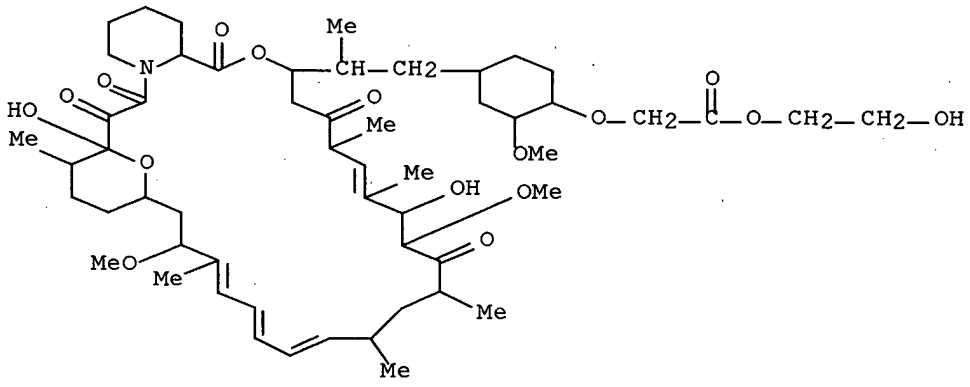
I

AB Novel O-alkylated derivs. of rapamycin I [X = O, H2; Y = O, H,OH; R1, R2 = H, (un)substituted alkyl, alkenyl, organosilyl; R3 = Me; R1R3 = alkylene], especially 40-O-alkylated derivs., have pharmaceutical utility, particularly as immunosuppressants. Rapamycin was treated with Me3CSiMe2OCH2CH2O3SCF3 and desilylated to give 40-O-(2-hydroxyethyl)rapamycin which had the following IC50 relative to rapamycin 1: mixed lymphocyte reaction 2.2, IL-6-dependent proliferation 2.8, macrophilin binding 3.4.

IT **159351-67-4P 159351-77-6P 159351-79-8P**
159351-80-1P 159351-82-3P 159351-83-4P
159351-84-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and immunosuppressant and neoplasm-inhibiting activity of)

RN 159351-67-4 CAPLUS

CN Rapamycin, 42-O-[2-(2-hydroxyethoxy)-2-oxoethyl]- (9CI) (CA INDEX NAME)

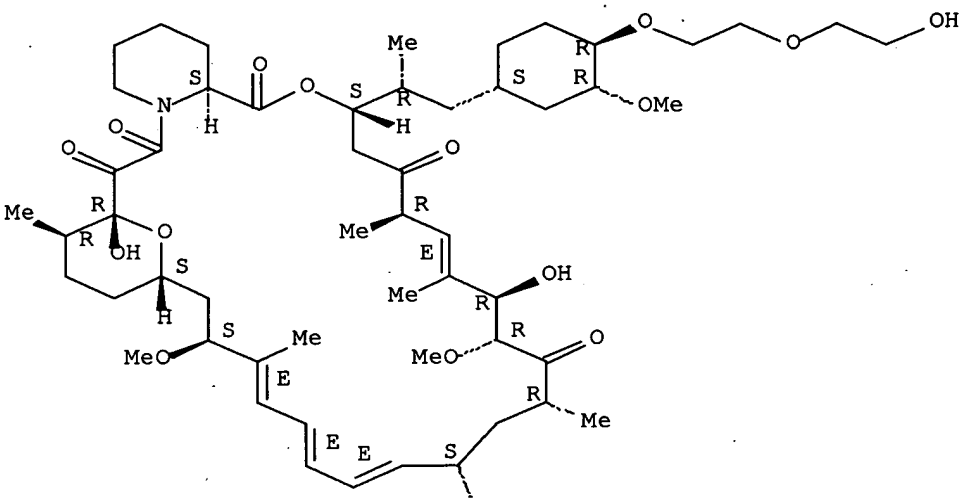


RN 159351-77-6 CAPLUS

CN Rapamycin, 42-O-[2-(2-hydroxyethoxy)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



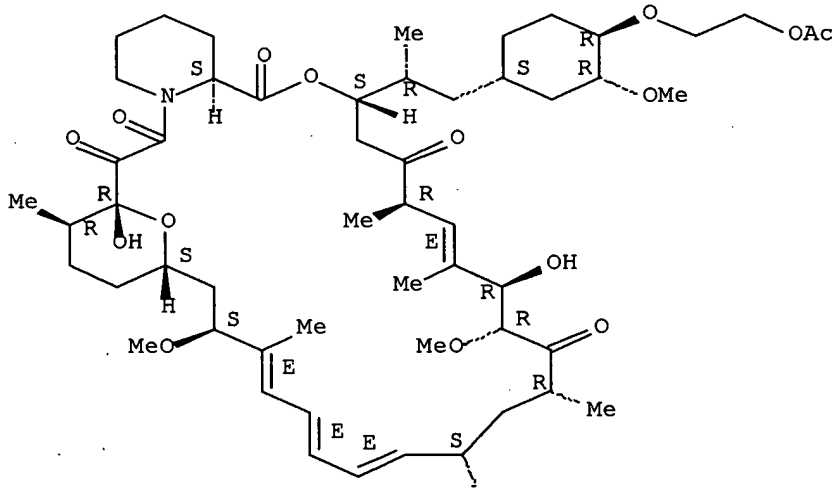
PAGE 2-A

Me

RN 159351-79-8 CAPLUS
CN Rapamycin, 42-O-[2-(acetyloxy)ethyl]- (9CI) (CA INDEX NAME)

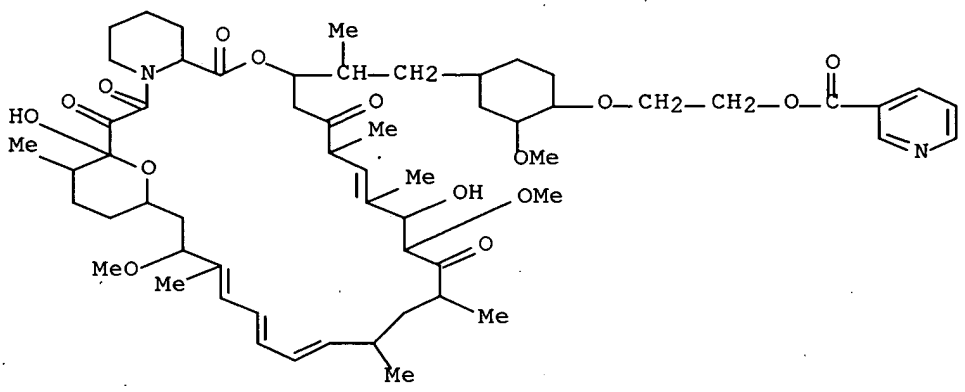
Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

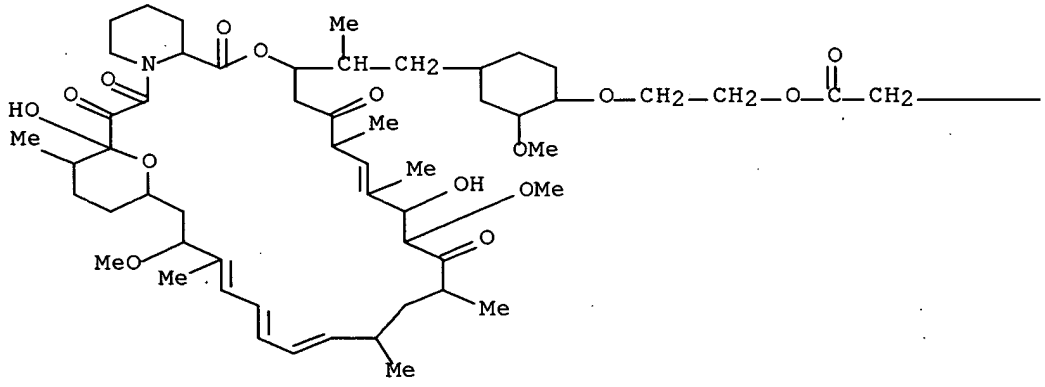


Me

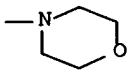
RN 159351-80-1 CAPLUS
CN Rapamycin, 42-O-[2-[(3-pyridinylcarbonyl)oxy]ethyl]- (9CI) (CA INDEX NAME)



RN 159351-82-3 CAPLUS
CN Rapamycin, 42-O-[2-[(4-morpholinylacetyl)oxy]ethyl]- (9CI) (CA INDEX NAME)

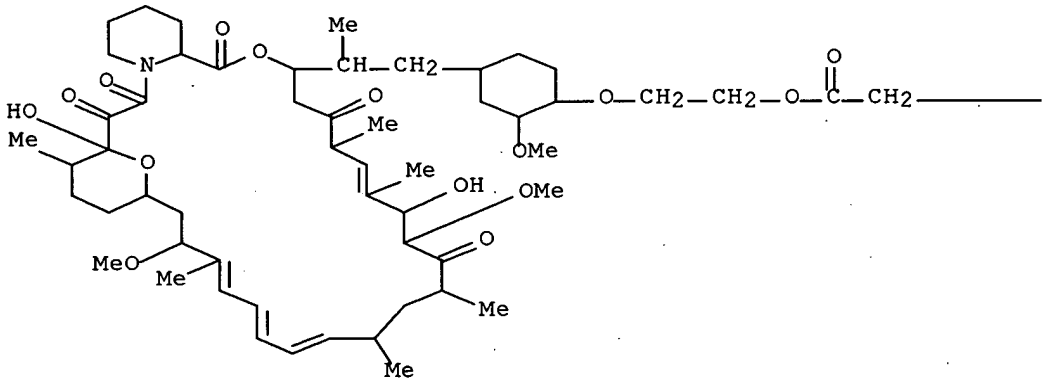


PAGE 1-B

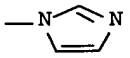


RN 159351-83-4 CAPLUS
CN Rapamycin, 42-O-[2-[(1H-imidazol-1-ylacetyl)oxy]ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

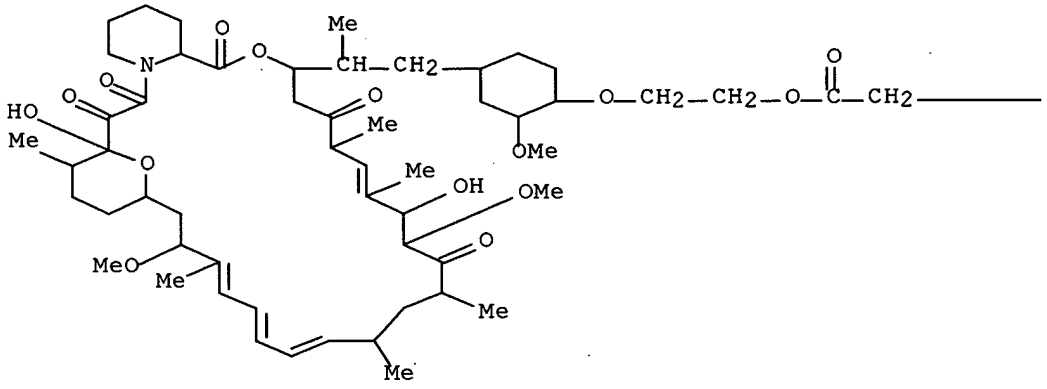


PAGE 1-B

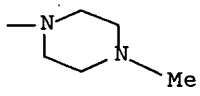


RN 159351-84-5 CAPLUS
CN Rapamycin, 42-O-[2-[[(4-methyl-1-piperazinyl)acetyl]oxy]ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

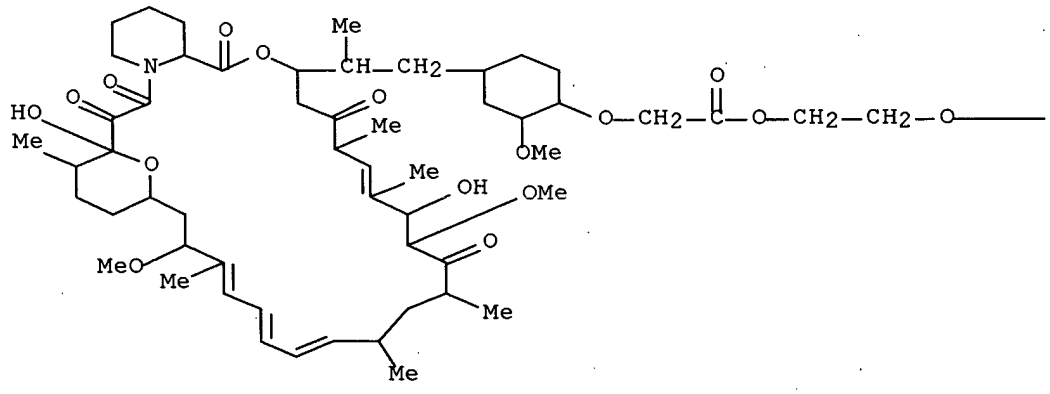


IT **159351-66-3P 159351-76-5P 159351-81-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of 40-O-alkylrapamycins)

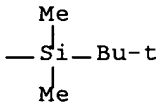
RN 159351-66-3 CAPLUS

CN Rapamycin, 42-O-[2-[2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]ethoxy]-2-oxoethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

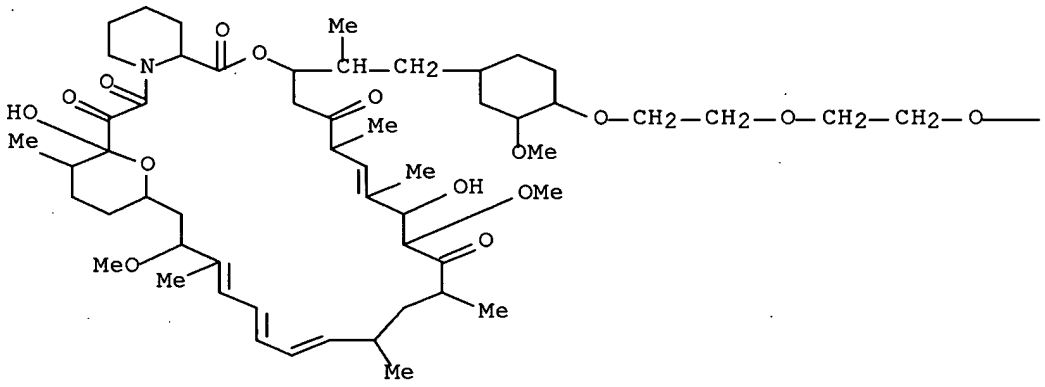


PAGE 1-B

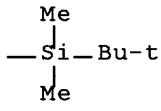


RN 159351-76-5 CAPLUS
CN Rapamycin, 42-O-[2-[2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]ethoxy]ethyl]- (9CI) (CA INDEX NAME)

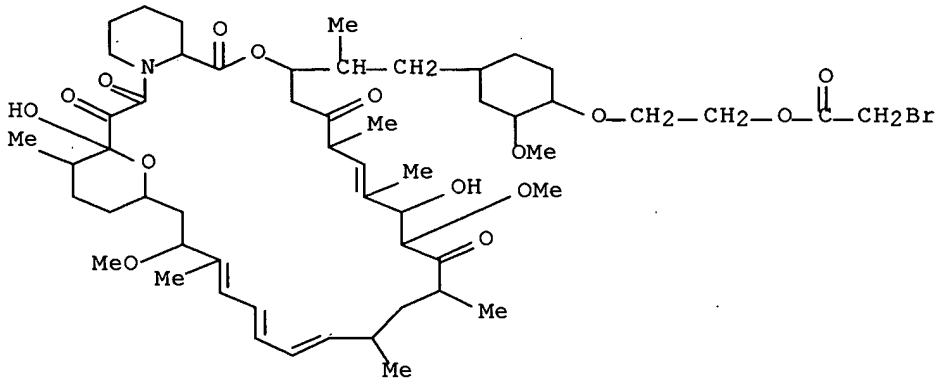
PAGE 1-A



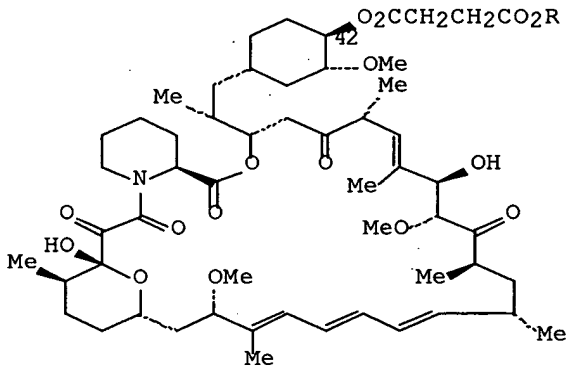
PAGE 1-B



RN 159351-81-2 CAPLUS
CN Rapamycin, 42-O-[2-[(bromoacetyl)oxy]ethyl]- (9CI) (CA INDEX NAME)



L6 ANSWER 34 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:435093 CAPLUS Full-text
DN 121:35093
TI Lipase mediated hydrolysis of rapamycin 42-hemisuccinate benzyl and methyl esters
AU Adamczky, Maciej; Gebler, John C.; Mattingly, Phillip G.
CS Abbott Diagn. Div., Abbott Lab., Abbott Park, IL, 60064, USA
SO Tetrahedron Letters (1994), 35(7), 1019-22
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 121:35093
GI

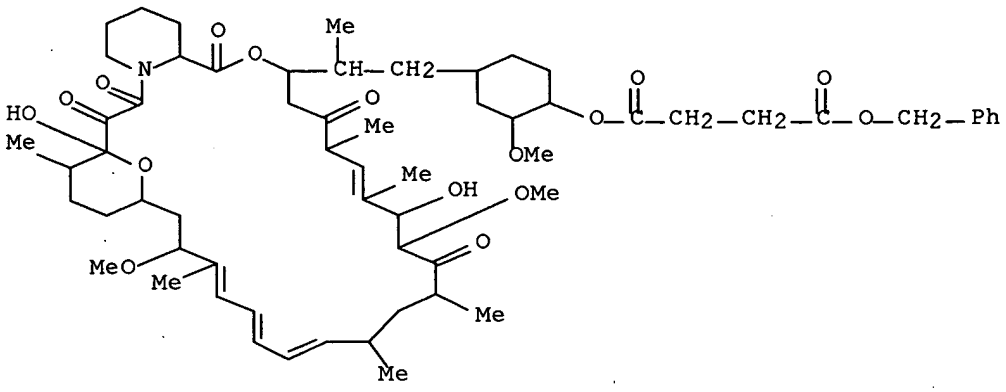


I

AB Benzyl and Me esters of rapamycin 42-hemisuccinate (I, R = CH2Ph, Me) were hydrolyzed under very mild conditions to the rapamycin hemisuccinate I (R = H) using lipase from Pseudomonas sp. This selective deprotection was performed on a ≥100 mg scale for both esters resulting in 50% isolated yield from the Me ester and 29% from the benzyl ester of the desired acid.

IT **143136-12-3P**, Benzyl rapamycin 42-succinate **155589-15-4P**
, Methyl rapamycin 42-succinate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and selective ester hydrolysis of)

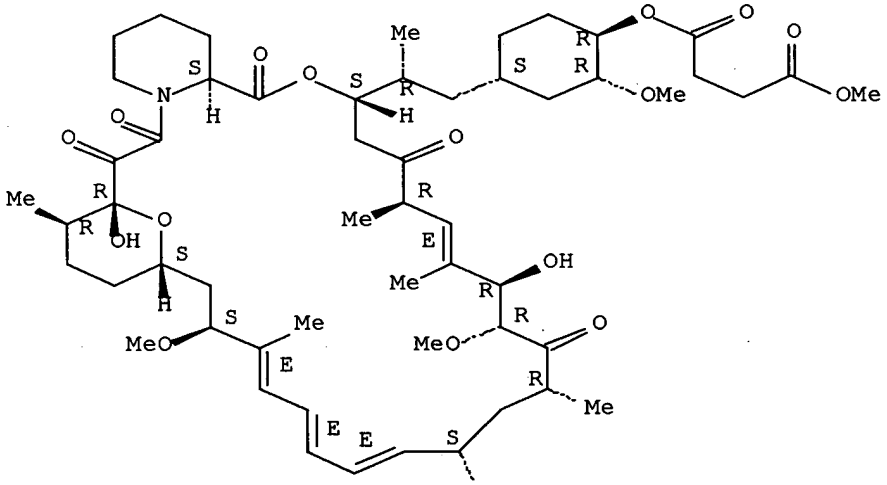
RN 143136-12-3 CAPLUS
CN Rapamycin, 42-(phenylmethyl butanedioate) (9CI) (CA INDEX NAME)



RN 155589-15-4 CAPLUS
CN Rapamycin, 42-(methyl butanedioate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

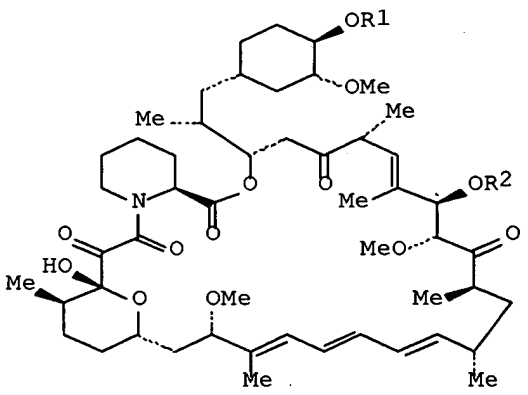


PAGE 2-A

L6 ANSWER 35 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:269937 CAPLUS Full-text
DN 120:269937
TI Preparation of rapamycin carbonate esters as immunosuppressant agents
IN Hu, David C.
PA American Home Products Corp., USA
SO U.S., 7 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5260300	A	19931109	US 1992-979072	19921119
	CA 2149669	AA	19940526	CA 1993-2149669	19931006
	WO 9411380	A1	19940526	WO 1993-US9548	19931006
	W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, UZ				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9453220	A1	19940608	AU 1994-53220	19931006
	EP 669923	A1	19950906	EP 1993-923281	19931006
	EP 669923	B1	19970416		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 08503210	T2	19960409	JP 1993-512073	19931006
	HU 73418	A2	19960729	HU 1995-1464	19931006
	AT 151769	E	19970515	AT 1993-923281	19931006
	ES 2100572	T3	19970616	ES 1993-923281	19931006
PRAI	US 1992-979072	A	19921119		
	WO 1993-US9548	W	19931006		

OS MARPAT 120:269937
GI

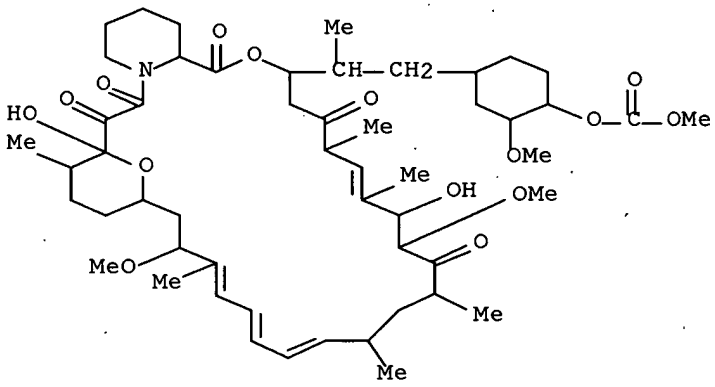


I

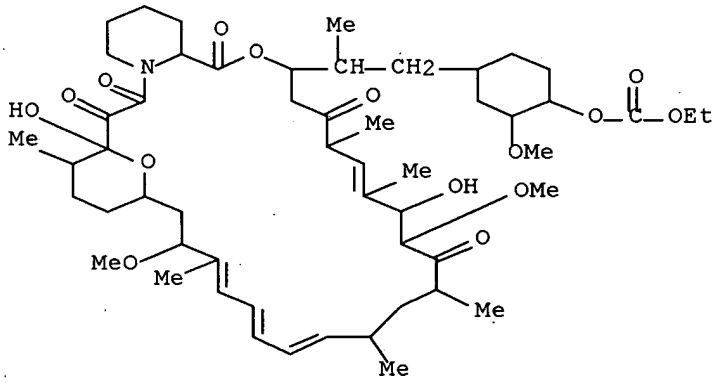
AB Title compds. I (R1, R2 = H, R3O2C wherein R3 = C1-3 alkyl where 1-3 H may be replaced by halo, C3-8 cycloalkyl, C2-6 alkenyl, Ar(CH2)n where n = 0-6 and Ar = (substituted) Ph, pyridinyl, indolyl, quinolyl, furanyl) or a salt thereof, are prepared To rapamycin in Et2O/THF was added pyridine and ClCO2CH2Ph to give after workup I (R1 = PhOCO, R2 = H) (II). In an in vitro standard pharmacol. test to measure lymphocyte proliferation as immunosuppressive activity, the IC50 of II was 0.32 nM.

IT **154492-08-7P 154492-10-1P 154492-14-5P**
154492-15-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as immunosuppressant)

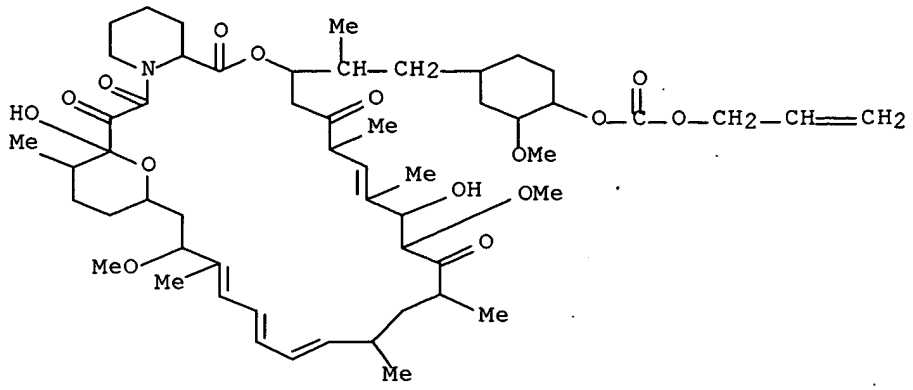
RN 154492-08-7 CAPLUS
CN Rapamycin, 42-(methyl carbonate) (9CI) (CA INDEX NAME)



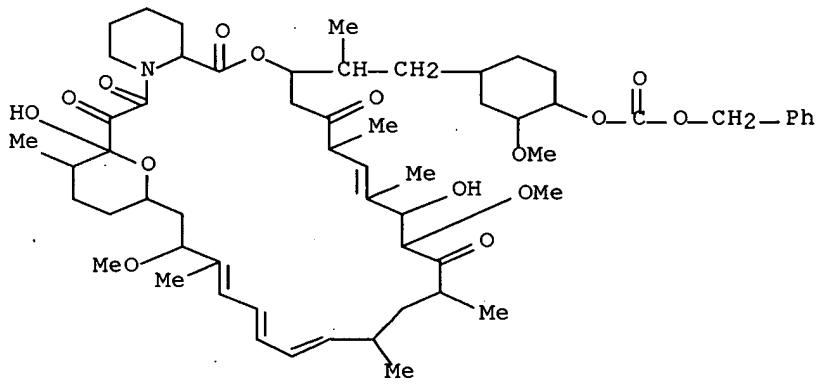
RN 154492-10-1 CAPLUS
CN Rapamycin, 42-(ethyl carbonate) (9CI) (CA INDEX NAME)



RN 154492-14-5 CAPLUS
CN Rapamycin, 42-(2-propenyl carbonate) (9CI) (CA INDEX NAME)



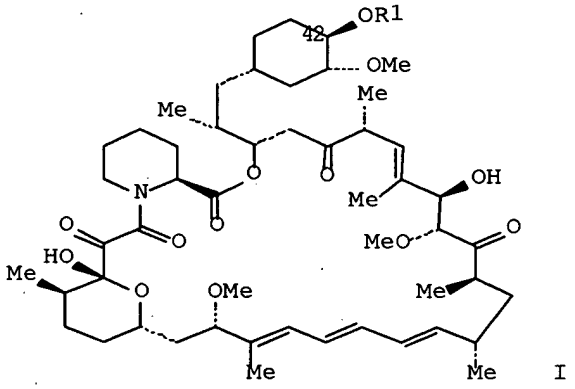
RN 154492-15-6 CAPLUS
CN Rapamycin, 42-(phenylmethyl carbonate) (9CI) (CA INDEX NAME)



L6 ANSWER 36 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:30610 CAPLUS Full-text
DN 120:30610
TI Rapamycin alkoxyesters for use as immunosuppressives, antiinflammatories, and antifungal agents
IN Hughes, Philip F.
PA American Home Products Corp., USA
SO U.S., 5 pp. Cont. of U.S. Ser. No. 598,270, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5233036	A	19930803	US 1992-839653	19920220
PRAI	US 1990-598270	B1	19901016		

OS MARPAT 120:30610
GI

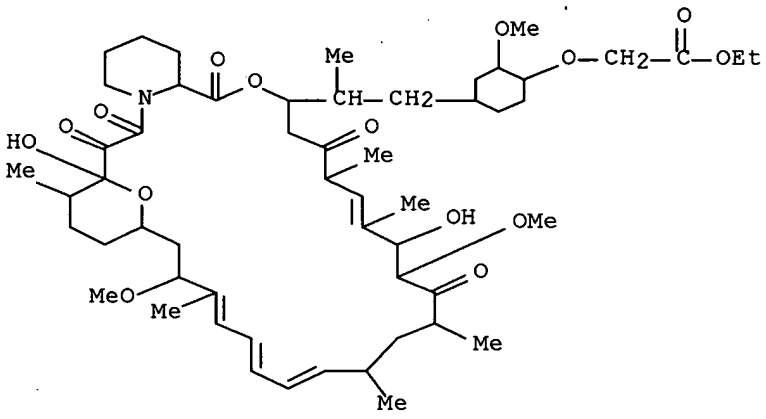


I

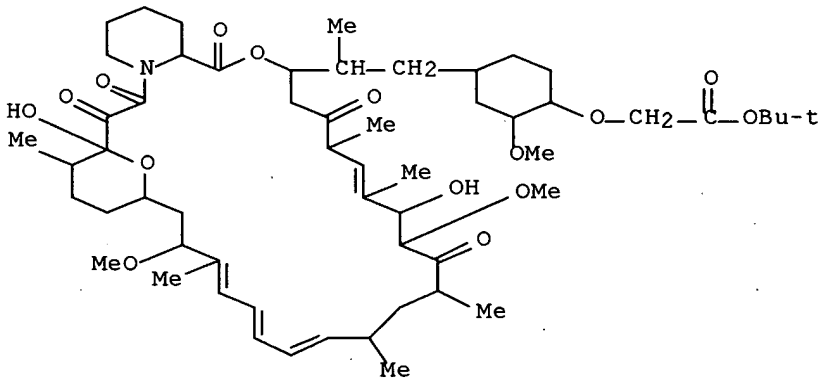
AB Title esters I [R1 = CH2CO2R2; R2 = H, C1-6 alkyl, (un)saturated C3-8 cycloalkyl, C7-10 aralkyl, (un)substituted Ph (1-3 substituents selected from C1-6 alkyl or alkoxy, OH, cyano, halo, NO2, C2-7 carbalkoxy, CF3, amino, carboxylic acid); or salts when R2 = H] are prepared as immunosuppressives, antiinflammatories, and/or antifungal agents. Rapamycin, i.e. I (R1 = H), was etherified by Et or tert-Bu diazoacetate in the presence of Rh(OAc)2 to give I [R1 = CH2CO2R2, R2 = Et (II) or tert-Bu (III)] in 23% and 26% yield, resp. Whether II had immunosuppressive activity was unclear from 3 standard tests. III was tested by 1 of the procedures and was active. II and III were active against 5 strains of Candida albicans, with MIC values (μg/mL) of 0.5 and 0.05, resp., against ATCC-10231 (cf. 0.003 for rapamycin).

IT **151477-91-7P**, 42-Deoxy-42-(2-ethoxy-2-oxoethoxy)rapamycin
151477-92-8P, 42-Deoxy-42-[2-(1,1-dimethylethoxy)-2-oxoethoxy]rapamycin
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as immunosuppressive, antiinflammatory, and/or antifungal)

RN 151477-91-7 CAPLUS
CN Rapamycin, 42-O-(2-ethoxy-2-oxoethyl)- (9CI) (CA INDEX NAME)



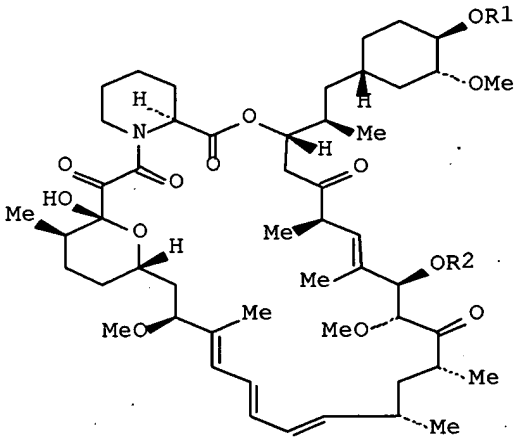
RN 151477-92-8 CAPLUS
CN Rapamycin, 42-O-[2-(1,1-dimethylethoxy)-2-oxoethyl]- (9CI) (CA INDEX NAME)



L6 ANSWER 37 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:80728 CAPLUS Full-text
DN 118:80728
TI Preparation of rapamycin alkoxymethyl ethers as immunosuppressant and antifungal agents
IN Caufield, Craig E.; Schiehser, Guy A.
PA American Home Products Corp., USA
SO U.S., 5 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5151413	A	19920929	US 1991-788682	19911106
PRAI US 1991-788682		19911106		

OS MARPAT 118:80728
GI

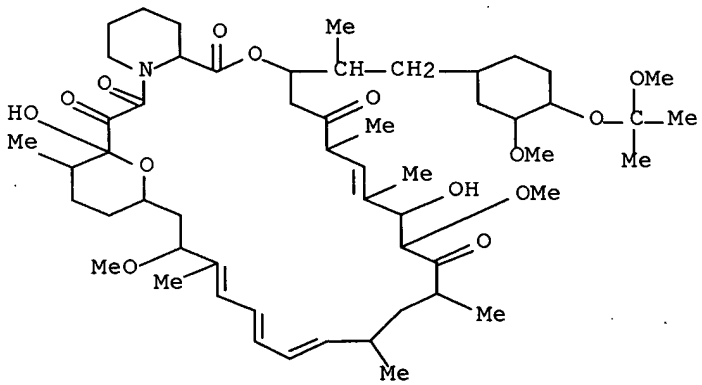


I

AB Title compds. [I; R1, R2 = H (R1 = H ≠ R2), CH2YX, CMe2YX, CHMeYX, L; L = 2-tetrahydrofuryl, -thienyl, -(thio)pyranyl, etc.; X = Me, (CH2)nMe, CH2CH2OMe, CH2CH2SiMe3, etc.; Y = O, S; n = 1-5] were prepared Thus, rapamycin was etherified with MeOCH:CH2 to give I (R1 = H, R2 = CHMeOMe) which had MIC of 0.025 μg/mL against Candida albicans ATCC 10231.

IT **145547-87-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as immunosuppressant and antifungal agent)

RN 145547-87-1 CAPLUS
CN Rapamycin, 42-O-(1-methoxy-1-methylethyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 38 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1992:571084 CAPLUS Full-text
DN 117:171084
TI Carboxylic acid esters of rapamycin
IN Caufield, Craig Eugene; Failli, Amedeo Arturo; Steffan, Robert John
PA American Home Products Corp., USA
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9205179	A1	19920402	WO 1991-US6824	19910919
	W: AU, FI, HU, JP, KR, SU				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	US 5130307	A	19920714	US 1991-657294	19910219
	CA 2051781	AA	19920320	CA 1991-2051781	19910918
	CA 2051782	AA	19920329	CA 1991-2051782	19910918
	AU 9186599	A1	19920415	AU 1991-86599	19910919
	AU 653175	B2	19940922		
	EP 549727	A1	19930707	EP 1991-919248	19910919
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 06501012	T2	19940127	JP 1991-516749	19910919
	HU 65763	A2	19940728	HU 1993-776	19910919
PRAI	US 1990-584833	A	19900919		
	US 1990-589878	A	19900928		
	US 1991-657294	A	19910219		
	WO 1991-US6824	A	19910919		

OS MARPAT 117:171084
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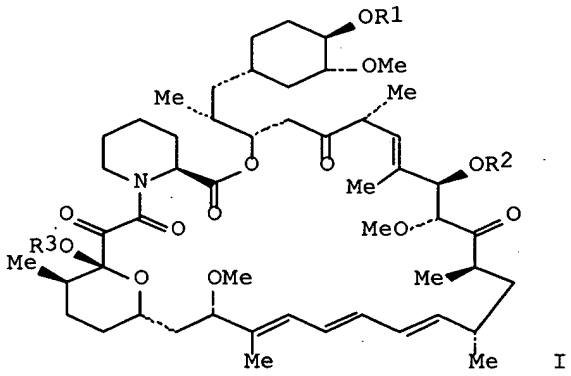
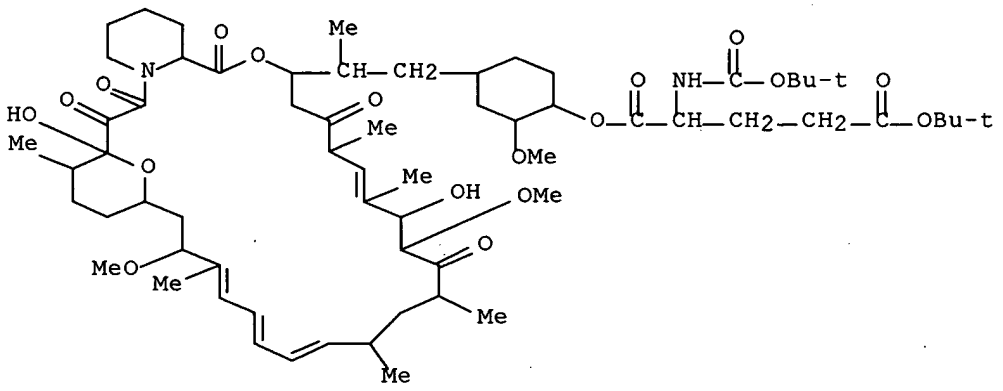


I

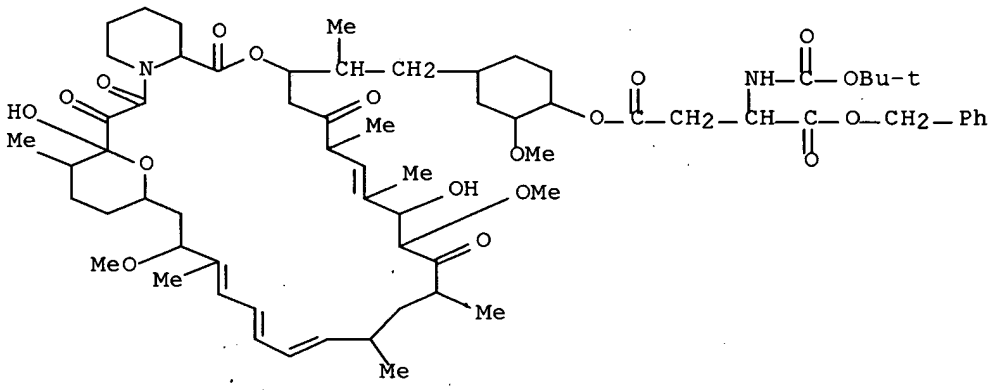
AB The title compds. I (R1-R3 = H, carboxyaminoalkanoyl, carboxyalkoxyalkanoyl, carboxyalkylthioalkanoyl, carboxyalkanoyl, carboxybenzoyl, carboxypyridylcarbonyl) were prepared by acylation of rapamycin (I; R1 - R3 = H). Thus, acylation of a CH2Cl2 solution of I (R1 - R3 = H) with PhCH2O2CCH2CH2CO2H in the presence of Me2N(CH2)3N:C:NEt.HCl and 4-dimethylaminopyridine gave a mixture of I [R1- R3 = PhCH2O2CCH2CH2CO; R1 = R2 = PhCH2O2CCH2CH2CO, R3 = H; R1 = PhCH2O2CCH2CH2CO, R2 = R3 = H (II)] which were separated by flash chromatog. In the comitagen-induced thymocyte proliferation test II had 3.27 times the immunosuppressant activity of I (R1-R3= H). The min. inhibitory concentration of II against several Candida albicans strains was 0.1-0.4 mg/mL cf I (R1-R3 = H) 0.003-0.025 mg/mL.

IT **143136-02-1P 143136-05-4P 143136-06-5P**
143136-12-3P 143136-14-5P
RL: PREP (Preparation)
(preparation and immunosuppressant and antifungal activities of)

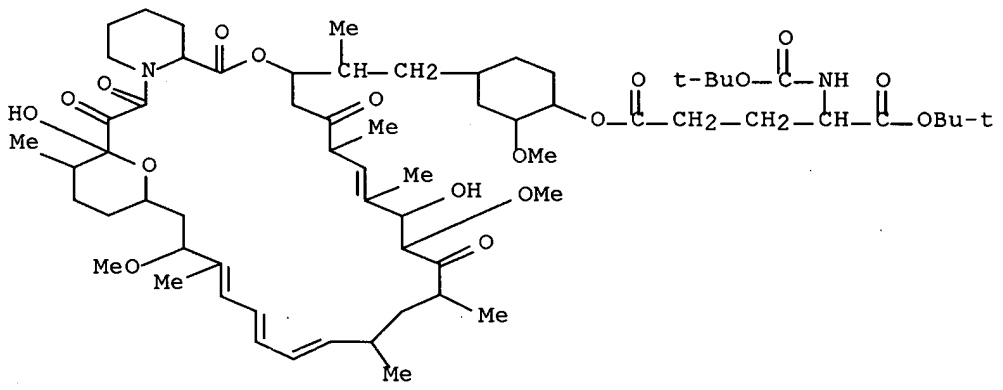
RN 143136-02-1 CAPLUS
CN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-, 5-(1,1-dimethylethyl) ester, 42-ester with rapamycin (9CI) (CA INDEX NAME)



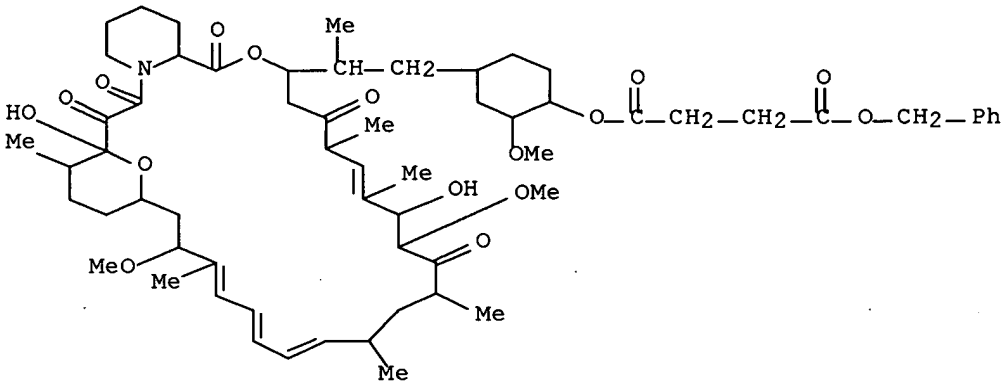
RN 143136-05-4 CAPLUS
CN L-Aspartic acid, N-[(1,1-dimethylethoxy)carbonyl]-, 1-(phenylmethyl) ester, 42-ester with rapamycin (9CI) (CA INDEX NAME)



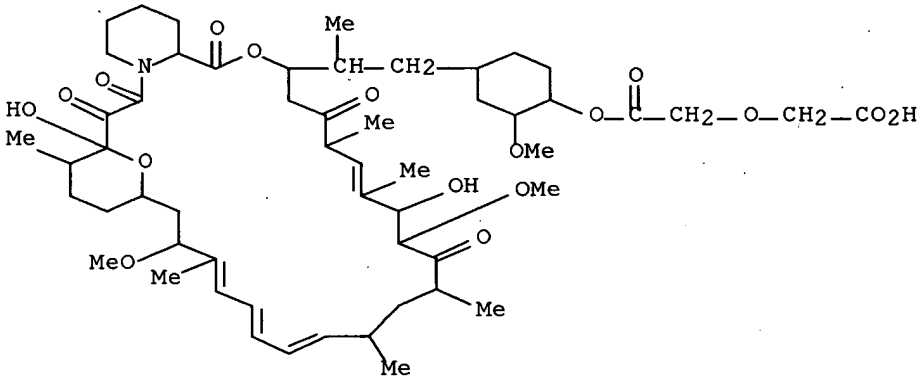
RN 143136-06-5 CAPLUS
CN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-, 1-(1,1-dimethylethyl) ester, 42-ester with rapamycin (9CI) (CA INDEX NAME)



RN 143136-12-3 CAPLUS
CN Rapamycin, 42-(phenylmethyl butanedioate) (9CI) (CA INDEX NAME)



RN 143136-14-5 CAPLUS
CN Rapamycin, 42-[(carboxymethoxy)acetate] (9CI) (CA INDEX NAME)



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L2              STR
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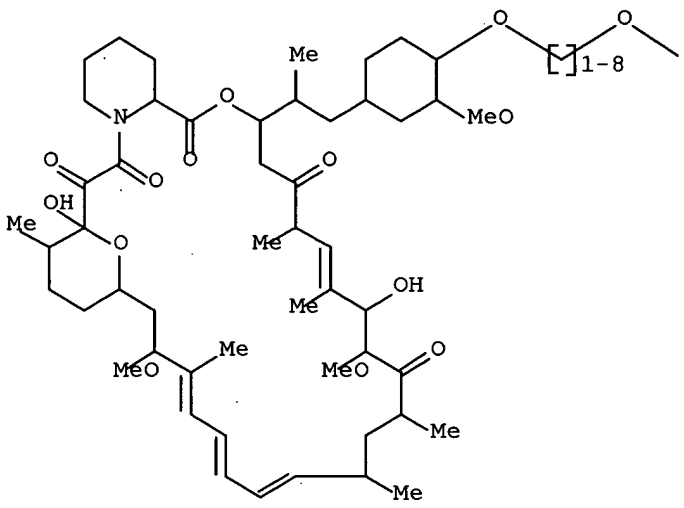


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     FILE 'STNGUIDE' ENTERED AT 18:01:08 ON 20 JUL 2005

     FILE 'REGISTRY' ENTERED AT 18:02:31 ON 20 JUL 2005
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L2              STRUCTURE UPLOADED
L3              QUE L2 AND L1
L4            2 S L3
L5           52 S L3 FUL

     FILE 'CAPLUS' ENTERED AT 18:03:01 ON 20 JUL 2005
L6           38 S L5

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                                                 ENTRY    SESSION
FULL ESTIMATED COST                             188.62     351.14

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                 ENTRY    SESSION
CA SUBSCRIBER PRICE                             -27.74     -27.74

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